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A 4-Year Retrospective Study: Clinical Outcomes of XEN45 in Patients with Glaucoma

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Keywords
Open-angle glaucoma · Microinvasive glaucoma surgery · XEN · Progression · Intraocular pressure · Retinal nerve fiber layer

Abstract

Introduction: The main purpose of the current study was to evaluate the long-term effectiveness and safety of XEN45 implant, either alone or in combination with cataract surgery, in patients with glaucoma. ***Methods:*** Retrospective and single center study conducted on consecutive patients who underwent a XEN45 implant, either alone or in combination with cataract surgery, between November 2016 and October 2021. The primary endpoint was the mean intraocular pressure (IOP) lowering from preoperative values. ***Results:*** Among the 230 screened patients, 206 eyes (176 patients) were included. Fifty-three (25.7%) eyes had undergone XEN alone and 153 (74.3%) eyes had undergone a combined procedure (XEN+phacoemulsification). The mean preoperative IOP was significantly higher in the XEN-alone (22.2 ± 5.9 mm Hg) than in the XEN+Phaco (19.8 ± 4.5 mm Hg) group ($p = 0.0035$). In the overall study population, the mean preoperative IOP was significantly lowered from 20.5 ± 5.0 mm Hg to 15.8 ± 4.4 at year-4, $p < 0.0001$. The mean preoperative (95% confidence interval) IOP was significantly lowered from 22.2 (20.6–23.8) mm Hg and 19.8 (19.1–20.6) mm Hg to 15.6 (12.2–16.9) mm Hg and 15.9 (15.2–16.5) mm Hg at year-4 in the XEN-alone and XEN+Phaco groups, respectively ($p < 0.0001$ each, respectively). The number of ocular hypotensive medications was significant reduced from 2.6 ± 1.0 drugs to 1.3 ± 1.3 drugs, with no significant differences between XEN-alone and XEN+Phaco groups ($p = 0.1671$). On the first postoperative day, 62 (30.1%) eyes presented some type of complication. Fifteen (7.3%) eyes underwent a needling procedure. ***Conclusion:*** XEN45, either alone or in combination with phacoemulsification, significantly lowered the IOP and reduced the need of ocular hypotensive medication in the long-term.

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Introduction

Over the last decade, glaucoma surgery has experienced significant advances. Among them, minimally or microinvasive glaucoma surgery (MIGS) devices have been developed as safer and less traumatic means of lowering IOP in patients with glaucoma [1].

The definition of the term MIGS has been evolving since its inception [2, 3], and the generally accepted definition of MIGS has been changing over the years [4]. Among the different MIGS devices, XEN gel stents obtained the CE mark in December 2015 and were approved by the Food and Drug Administration (FDA) in November 2016 [5]. Although many studies have been published evaluating the effectiveness and safety of XEN45 implant [6–20], data evaluating its long-term clinical outcomes are very limited [11, 17]. The main purpose of the current study was to evaluate the long-term effectiveness and safety of XEN45 implant, either alone or in combination with cataract surgery, in patients with glaucoma.

Methods

Design

Retrospective and single center study conducted on consecutive patients who underwent a XEN45 implant, either alone or in combination with cataract surgery, between November 2016 and October 2021.

Study Participants

Patients aged ≥18 years old with insufficiently medically controlled early to advanced glaucoma, according to Hodapp et al. [21]; intolerance to topical hypotensive treatments; or poor treatment adherence, who underwent a XEN45 implant procedure, either alone or in combination with cataract surgery, were included in the study. Patients with closed-angle (narrow angle patients were included if, in surgeon opinion, there was enough space to implant the device safely); severe conjunctival problems; phacodonesis; progressive retinal or optic nerve disease of any cause; or history of major ocular surgery (except phacoemulsification) within the previous 6 months were excluded of the study.

Study Groups

The study sample was divided in two groups: XEN, eyes who underwent XEN implant alone; XEN+Phaco, eyes who underwent XEN gel stent implantation combined with phacoemulsification surgery.

Surgical Technique

All the surgical procedures were performed, under topical anesthesia. All surgeries were performed with mitomycin-C (MMC) (dose 0.1 mg/mL), which was injected intra-tenon in the supero-nasal quadrant. The device was placed in the superior nasal quadrant using a standard *ab interno* technique [12].

Definitions

Surgical success was defined as an IOP lowering from preoperative values ≥20% and an IOP absolute value between 6 and 18 mm Hg, without (complete success) or with (qualified success) antiglaucoma medications. Failure was defined as an IOP >18 mm Hg or a <20% reduction of IOP from baseline at the end of the follow-up period, need for additional glaucoma surgery, or vision threatening complications that led to severe loss of visual acuity (light perception or worse). Patients with an IOP <6 mm Hg for more than two consecutive visits were also considered a failure. Needling or surgical bleb revision, as needed, was indicated in those cases of failure of the procedure due to fibrosis or encapsulation of the bleb that did not respond to massage in the slit lamp and topical hypotensive medications.

Outcomes

The primary endpoint was the mean IOP lowering from preoperative values. Secondary endpoints included the mean IOP at the last follow-up visit; reduction in number of ocular hypotensive medications from baseline; proportion of eyes achieving a final IOP ≤12 mm Hg; ≤14 mm Hg; ≤16 mm Hg; ≤18 mm Hg; or ≤20 mm Hg with and without medications irrespective of the preoperative IOP lowering); and incidence of adverse events (AEs).

Statistical Analysis

Statistical analysis was performed with the MedCalc® Statistical Software version 22.021 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2024). Mean and standard deviation; mean and 95% confidence interval (95% CI); median and interquartile range; and number (percentage) were used as appropriated.

Data were tested for normal distribution using a D'Agostino-Pearson test. The last-observation-carried-forward method was used to impute missing data.

The repeated measures ANOVA or a Friedman's two-way analysis test, as appropriate, was used to assess the changes in IOP and in number of antiglaucoma medications. Post hoc analysis for pairwise comparisons was done with the Scheffé's method (ANOVA) or the Conover method (Friedman).

Repeated analysis of covariance (MANCOVA) was performed to assess the changes in IOP between study groups. The model included "type of surgery" (XEN alone or combined surgery) as a factor and age, preoperative IOP, number of preoperative ocular hypotensive medications, and pachymetry as covariates.

The Mann-Whitney U test was used for testing preoperative differences between study groups. Categorical variables were compared using a χ^2 test and a Fisher's exact test, as needed. p value of less than 0.05 was considered significant.

Results

Study Sample

Among the 230 screened patients, 206 eyes (176 patients) were included. Fifty-three (25.7%) eyes had undergone XEN alone and 153 (74.3%) eyes had undergone a combined procedure (XEN + phacoemulsification).

Table 1. Main preoperative demographic and clinical characteristics of the study population

	Overall (*n* = 206)	XEN alone (*n* = 53)	XEN+phaco (*n* = 153)	*p* value[a]
Age, years				0.7368
Mean (SD)	74.6 (10.8)	74.4 (9.9)	74.6 (11.1)	
Median (IqR)	76.9 (68.6–82.0)	77.1 (66.5–81.3)	76.8 (69.0–82.1)	
Sex, *n* (%)				1.0000[b]
Women	114 (55.3)	29 (54.7)	85 (55.6)	
Men	92 (44.7)	24 (45.39	68 (44.4)	
Race, *n* (%)				0.7620[c]
Caucasian	203 (98.5)	52 (98.1)	151 (98.7)	
Eye, *n* (%)				0.2027[b]
Right	112 (54.4)	33 (62.3)	79 (51.6)	
Left	94 (45.6)	20 (37.7)	74 (48.4)	
Glaucoma type, *n* (%)				
POAG	148 (73.3)	33 (62.3)	115/77.2)	
NTG	7 (3.5)	5 (9.4)	2 (1.3)	
PEX	33 (16.3)	12 (22.6)	21 (14.1)	0.2587[c]
PACG	9 (4.5)	2 (3.8)	7 (4.7)	
Other	5 (2.5)	1 (1.9)	4 (2.7)	
PS, *n* (%)				0.0002[b]
Yes	37 (18.6)	19 (37.3)	18 (12.2)	
No	162 (81.4)	32 (62.7)	130 (87.8)	
Lens status, *n* (%)				<0.0001[b]
Phakic	175 (85.0)	22 (41.5)	153 (100.0)	
Pseudophakic	31 (15.0)	31 (58.5)	0 (0.0)	
Baseline IOP[d], mm Hg				0.9828
Mean (SD)	28.8 (7.8)	28.1 (6.0)	29.0 (8.2)	
Median (IqR)	28.0 (24.0–33.0)	30.0 (24.3–32.0)	28.0 (23.4–34.0)	
Preoperative IOP, mm Hg				0.0035
Mean (SD)	20.5 (5.0)	22.2 (5.9)	19.8 (4.5)	
Median (IqR)	20.0 (17.0–23.0)	21.0 819.0 to 25.0)	19.0 (16.0–22.0)	
NOHM, *n*				0.7601
Mean (SD)	2.6 (1.0)	2.6 (1.2)	2.6 (0.9)	
Median (IqR)	3.0 (2.0–3.0)	3.0 (2.0–3.0)	3.0 (2.0–3.0)	
Pachymetry[e], µm				0.2143
Mean (SD)	533.0 (36.9)	539.7 (38.5)	530.8 (36.2)	
Median (IqR)	531.0 (507.8–558.0)	534.0 (512.5–550.2)	530.5 (506.0–556.0)	
BCVA[f]				0.1539
Mean (SD)	0.69 (0.26)	0.73 (0.28)	0.68 (0.26)	
Median (IqR)	0.70 (0.50–0.90)	0.80 (0.53–1.0)	0.70 (0.50–0.90)	
VF damage[g], dB				
MD				0.0733
Mean (SD)	−8.3 (8.6)	−10.4 (9.1)	−7.7 (0.4)	
Median (IqR)	−5.7 (−12.6 to −1.7)	−8.4 (−16.0 to −2.9)	−4.7 (−11.3 to −1.4)	
MSD				0.4427
Mean (SD)	5.5 (3.7)	5.9 (3.7)	5.4 (3.7)	
Median (IqR)	4.2 (2.1–8.6)	5.9 (2.0–9.1)	4.0 (2.1–8.5)	
VFI				
Mean (SD)	71.2 (33.8)	61.4 (36.8)	73.8 (32.6)	0.0822
Median (IqR)	86.0 (51.0–98.0)	73.5 (25.0–97.0)	89.0 (63.0–98.0)	
ARNFL[h], µm				0.5675
Mean (SD)	70.1 (21.6)	68.6 (20.6)	70.5 (21.9)	
Median (IqR)	72.0 (53.0–86.0)	73.0 (52.3–80.8)	71.0 (53.0–88.3)	

SD, standard deviation; IqR, interquartile range; POAG, primary open-angle glaucoma; NGT, normal tension glaucoma; PEX, pseudoexfoliative glaucoma; PACG, primary angle-closure glaucoma; PS, previous surgery; NOHM, number of ocular hypotensive medication; BCVA, best corrected visual acuity; VF, visual field; MD, mean defect; MSD, mean standard deviation; VFI, visual field index; ARNFL., average retinal nerve fiber layer thickness. [a]Mann-Whitney U test. [b]Fisher exact test. [c]χ^2 test. [d]IOP at diagnosis. Available in 106 eyes. [e]Available in 185 eyes. [f]Snellen. [g]Available in 173 eyes. [h]Available in 192 eyes.

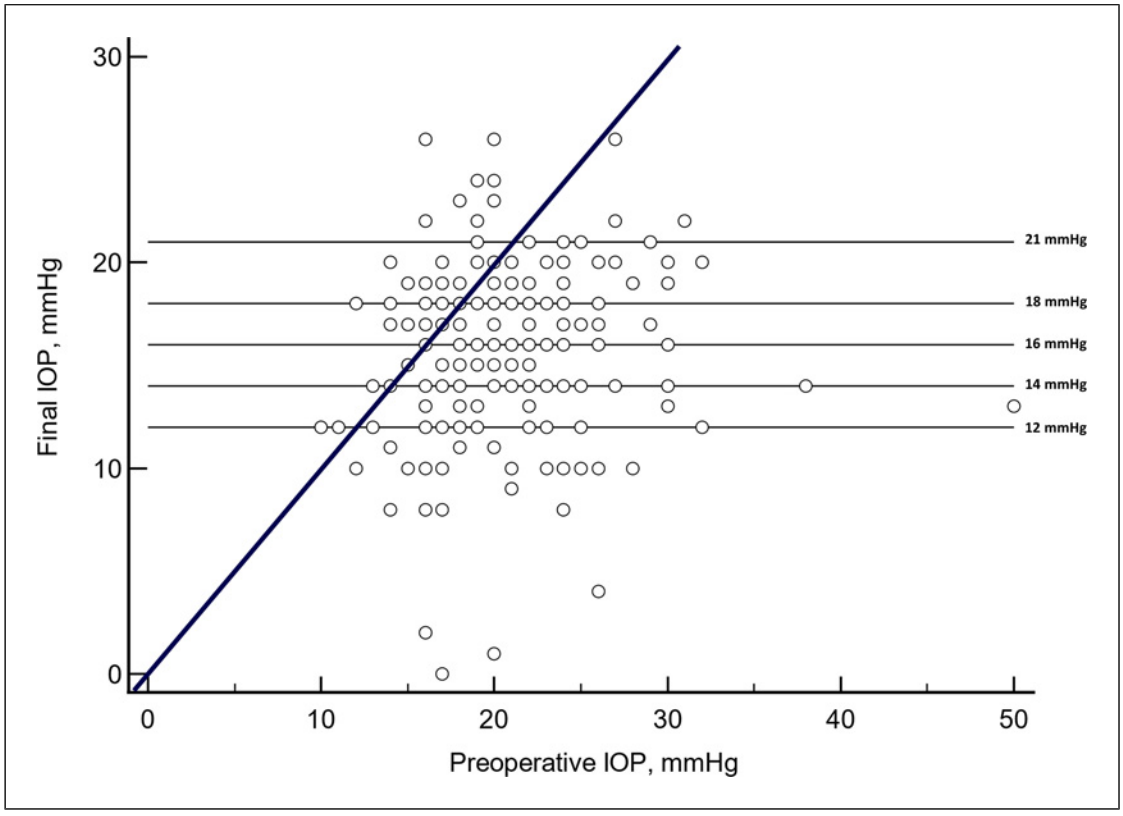

Fig. 1. Scatter plot of the preoperative and month-48 intraocular pressure (IOP) (mean difference: −4.7 mm Hg; 95% CI: −5.5 mm Hg to −3.8 mm Hg, $p < 0.0001$, repeated ANOVA and the Greenhouse-Geisser correction test).

Preoperative Demographic and Clinical Characteristics

In the overall study sample, the mean age was 74.6 ± 10.8 years, with no significant differences between study groups ($p = 0.7368$). One hundred-fourteen (55.3%) were women; 203 (98.5%) were Caucasian; and 148 (73.3%) eyes were diagnosed with primary open-angle glaucoma. The Table 1 summarizes the main preoperative demographic and clinical characteristics.

With the exception of the intraocular pressure (IOP) and the proportion of eye with previous surgery, there were no significant differences in any of the preoperative variables between XEN-alone and XEN+Phaco groups. The mean preoperative IOP was significantly higher in the XEN-alone (22.2 ± 5.9 mm Hg) than in the XEN+Phaco (19.8 ± 4.5 mm Hg) group (Hodges-Lehmann median differenced: 2.0 mm Hg; 95% CI: 1.0 mm Hg–4.0 mm Hg, $p = 0.0035$). The proportion of eyes who had undergone a previous surgical procedure was significantly greater in the XEN-alone group (37.3%) than in the XEN+Phaco group (12.2%), $p = 0.0002$.

Intraocular Pressure

In the overall study population, the mean preoperative IOP was significantly lowered from 20.5 ± 5.0 mm Hg to 15.8 ± 4.4 mm Hg (mean difference: −4.7 mm Hg; 95% CI: −5.5 mm Hg to −3.8 mm Hg, $p < 0.0001$, repeated ANOVA).

Data were plotted from preoperative IOP on the X-axis and final visit IOP on the Y-axis to make an overall visual assessment (Fig. 1). The mean preoperative (95% CI) IOP was significantly lowered from 22.2 (20.6–23.8) mm Hg and 19.8 (19.1–20.6) mm Hg to 15.6 (12.2–16.9) mm Hg and 15.9 (15.2–16.5) mm Hg in the XEN-alone and XEN+Phaco groups, respectively ($p < 0.0001$ each, repeated ANOVA). The mean IOP at day 1, week 1, and month 1 was significantly lower in the XEN-alone than in the XEN+Phaco group ($p < 0.0001$, $p = 0.0036$, and $p = 0.0041$, respectively). No significant differences were observed at any of the other time-points measured between the two study groups (Fig. 2).

After adjusting for different covariates (age, preoperative IOP, preoperative number of ocular hypotensive medications, and pachymetry), the IOP lowering was significantly greater in the XEN-alone group at day 1, week 1, month 1, and month 6 (Table 2). At the last follow-up visit, 41 (19.9%)

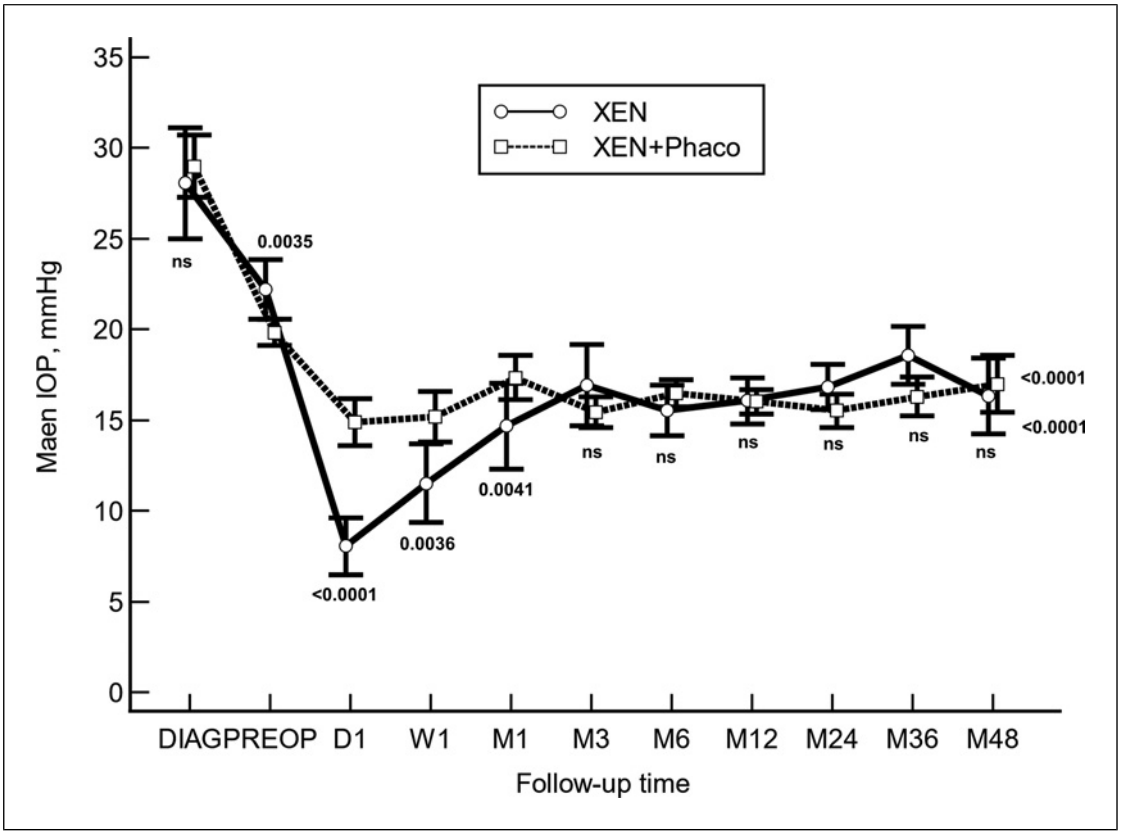

Fig. 2. Mean intraocular pressure (IOP) in the XEN-añone and XEN+Phaco eyes throughout study follow-up. Vertical bars represent standard deviation. Intergroup statistical significance, at the different time point measurements, was determined using the one-way ANOVA test with the Scheffé's method. As compared to baseline, the mean IOP was significantly reduced, at every time point measured, $p < 0.001$ (repeated measures ANOVA and the Greenhouse-Geisser correction). DIAG, intraocular pressure at diagnosis; Preop, preoperative; D, day; W, week; M, month.

eyes had an IOP ≤12 mm Hg; 119 (57.8%) an IOP ≤16 mm Hg; and 186 (90.3%) eyes and IOP ≤20 mm Hg (Table 3). Success rate was 50.0% (103/206) eyes in the overall study sample, 60.4% (32/53) eyes in the XEN-alone group and 46.4% (71/153) eyes in the XEN+Phaco group ($p = 0.2151$).

Ocular Hypotensive Medications

The mean preoperative number of ocular hypotensive medications was significantly reduced from 2.6 ± 1.0 drugs to 1.3 ± 1.3 drugs at the last follow-up visit. There were no statistically significantly differences in mean ocular hypotensive medication reduction between the XEN-alone (1.2 ± 1.4 drugs) and the XEN+Phaco (1.5 ± 1.3 drugs) groups, $p = 0.1671$.

Survival Analysis

Kaplan-Meier survival analysis indicated no significant differences in the success rate between the XEN-alone and the XEN+Phaco groups (mean hazard ratio: 1.30; 95% CI: 0.99 to 1.72; $p = 0.0623$) (Fig. 3).

Safety

On the first postoperative day, 62 (30.1%) eyes presented some type of complication. Most of the complications resolved during the first week with medical treatment and without sequelae (Table 4). The most commonly reported postoperative complication was transient subclinical hypotony in 28 (13.6%) eyes, followed by peak hypertensive (IOP >30 mm Hg) in 12 (5.8% 9 eyes).

The incidence rate of AEs was significantly higher in the XEN45+Phaco group than in the XEN45-alone group at postoperative day 1, but not in subsequent visits (Table 4). No complication extended beyond month 6. In all cases, it was resolved satisfactorily with treatment.

Throughout the study follow-up, 80 (38.8%) eyes underwent some type of surgical procedure. Fifteen (7.3%) eyes (7 eyes in the XEN-alone group and 8 eyes in the XEN+Phaco group) underwent a needling procedure (mean time for needling 202.5 ± 172.3 days; without significant differences between groups, $p = 0.5893$) and 36 (17.5%) eyes

Table 2. Adjusted mean intraocular pressure (IOP) difference from preoperative values in XEN-alone and XEN + phacoemulsification groups

	Mean IOP lowering			
	XEN alone	XEN + phaco	difference	*p* value[a]
Day 1				<0.0001
Mean (SE)	12.4 (1.2)	5.1 (0.6)	7.3 (1.4)	
95% CI	10.1 to 14.8	3.9 to 6.4	4.6 to 10.0	
Week 1				0.0013
Mean (SE)	9.7 (1.3)	4.6 (0.7)	5.1 (1.6)	
95% CI	7.0 to 12.3	3.1 to 6.1	2.0 to 8.1	
Month 1				0.0115
Mean (SE)	6.3 (1.2)	2.7 (0.7)	3.6 (1.4)	
95% CI	3.9 to 8.7	1.4 to 4.1	0.8 to 6.3	
Month 3	3.8 (1.0)	4.9 (0.5)	−1.1 (1.1)	0.2956
Mean (SE)	1.9 to 5.7	3.9 to 6.0	−3.3 to 1.0	
95% CI				
Month 6				0.0105
Mean (SE)	5.8 (0.7)	3.7 (0.4)	2.1 (0.8)	
95% CI	4.4 to 7.1	3.0 to 4.5	0.5 to 3.6	
Month 12				0.3319
Mean (SE)	4.8 (0.6)	4.1 (0.4)	0.7 (0.7)	
95% CI	3.6 to 6.0	3.3 to 4.8	−0.7 to 2.2	
Month 24				0.3315
Mean (SE)	3.8 (0.7)	4.7 (0.5)	−0.9 (0.9)	
95% CI	2.4 to 5.2	3.7 to 5.7	−2.6 to 0.9	
Month 36				0.0571
Mean (SE)	1.7 (0.8)	3.7 (0.7)	−2.0 (1.1)	
95% CI	0.2 to 3.2	2.4 to 5.1	−4.1 to 0.1	
Month 48				0.1237
Mean (SE)	−5.1 (1.0)	2.3 (1.3)	2.9 (1.8)	
95% CI	3.0 to 7.3	0.4 to 4.9	−0.9 to 6.6	
Final				0.4595
Mean (SE)	4.8 (0.7)	4.2 (0.4)	0.6 (0.8)	
95% CI	3.5 to 6.1	3.5 to 5.0	−0.9 to 2.1	

The model included "Surgery" (XEN-alone vs. XEN + Phaco) as a factor and age, preoperative IOP, preoperative number of ocular hypotensive drugs, and pachymetry as covariates. [a]Analysis of covariance (ANCOVA).

Table 3. Proportion of eyes who achieved different intraocular pressure (IOP) targets irrespective of the IOP reduction, with and without treatment, at the last follow-up visit

	Final IOP (n = 206)	
IOP	with ocular hypotensive medication, *n* (%)	without ocular hypotensive medication, *n* (%)
≤12	19 (9.3)	22 (10.7)
≤14	39 (18.9)	45 (21.8)
≤16	59 (28.6)	60 (29.1)
≤18	83 (40.3)	70 (34.0)
≤20	103 (50.0)	83 (40.3)

IOP, intraocular pressure.

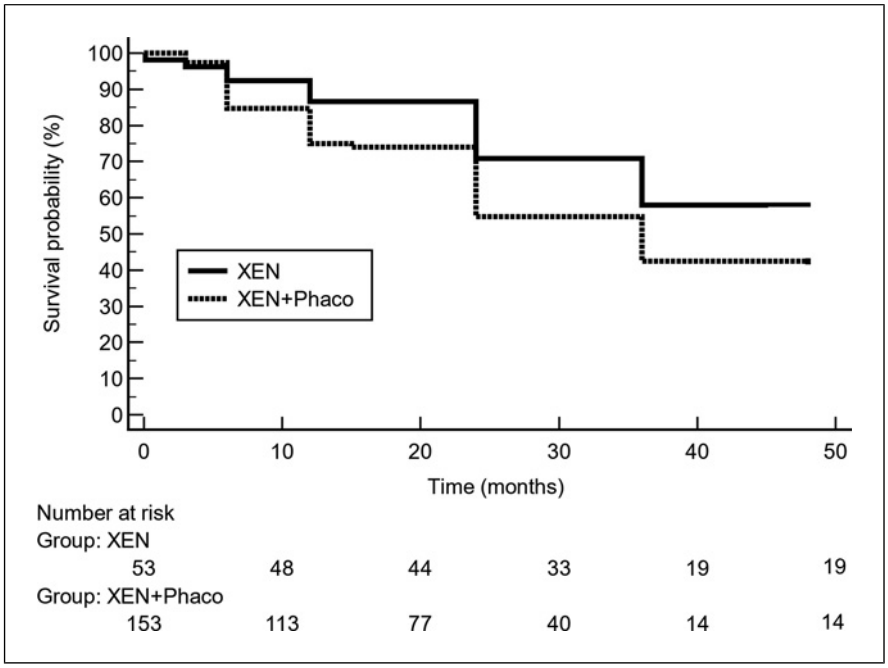

Fig. 3. Kaplan-Meier survival analysis. Mean hazard ratio: 1.30; 95% CI: 0.99 to 1.72; $p = 0.0623$.

Table 4. Postoperative complications

Complication, *n*	Day 1 (*n* = 62)		Week 1 (*n* = 31)		Month 1 (*n* = 24)		Month 3 (*n* = 10)	
	XEN45	XEN45+phaco	XEN45	XEN45+phaco	XEN45	XEN45+phaco	XEN45 alone	XEN45+phaco
Transient hypotony[a]	18	10	10	8	4	5	1	2
IOP spikes[b]	0	12	1	6	2	6	2	2
Hyphema	2	7	1	1	0	0	0	0
Corneal edema	0	3	0	0	0	0	0	0
AC blood[c]	1	0	0	0	0	0	0	0
Macular edema	1	3	0	0	0	0	0	1
Shallow AC	1	1	1	2	0	1	0	1
Bleb leakage	0	2	0	0	0	3	0	1
Choroidal detachment	1	0	1	0	2	1	0	0
Overall	24	38	14	17	8	16	3	7

IOP, intraocular pressure; AC, anterior chamber. Statistical significance was calculated with χ^2 test: day 1 ($p = 0.0033$); week 1 ($p = 0.2996$); month 1 ($p = 0.3732$); month 3 ($p = 0.7241$). [a]Subclinical. [b]IOP >30 mm Hg. [c]Approximately ½ of the anterior chamber.

underwent bleb revision (7 eyes in the XEN-alone group and 29 eyes in the XEN+Phaco group, $p = 0.0002$). Four (1.9%) eyes (1 eye in the XEN-alone group and 3 eyes in the XEN+Phaco group) underwent a device replacement, and 25 (12.1%) eyes underwent additional surgeries (Trabeculectomy or glaucoma drainage devices) (12 eyes in the XEN-alone group and 13 eyes in the XEN+Phaco group).

Discussion

According to the results of the current study, XEN45 stent, either alone or in combination with phacoemulsification, significantly lowered the IOP and reduced the number of ocular hypotensive medications in patients with glaucoma in a real clinical setting. Interestingly, this study

Table 5. A comparison of the clinical outcomes between the current study and the available evidence

Study	Type of study	*N*	Length of study, months	Preoperative IOP, mm Hg	Final IOP	IOP lowering, %	Mean reduction in ocular hypotensive medication
Lenzhofer et al. [11]	Prospective	34	48	22.5±4.2	13.4±3.1	40.4	1.2
Gillmann et al. [17]							
XEN alone	Prospective	26	36	21.0±7.4	12.9±2.9	38.6	2.1
XEN+Phaco	Prospective	76	36	20.0±6.9	12.9±3.4	35.5	1.4
Reitsamer et al. [22]	Retrospective	76	36	20.7±5.1	13.9±4.3	32.9	1.4
Gabbay et al. [23]	Retrospective	205	36	22.6±7.0	14.0±2.9	38.1	2.0
Nuzzi et al. [24]	Retrospective	23	36	24.9±6.1	19.6±2.1	21.3	Not reported
Current study							
XEN alone	Retrospective	53	48	22.2±5.9	15.6±4.9	26.5	1.1
XEN+Phaco	Retrospective	153	48	19.8±4.5	15.9±4.2	16.9	1.5

IOP, intraocular pressure; *N*, number of eyes.

suggested that in the short term, the IOP lowering effect of XEN alone was higher than that observed in patients undergoing XEN combined with phacoemulsification, although the IOP lowering effect equals from month 1. Additionally, it should be highlighted the relatively high proportion of patients achieving low target IOPs, with 119 (57.8%) eyes achieving an IOP ≤16 mm Hg.

Success rate was 50.0% (103/206) eyes in the overall study sample, with not significant differences between XEN and XEN+Phaco groups. From a clinical point of view, few studies have reported the long-term efficacy, in terms of IOP lowering and the amount of ocular hypotensive medications reduction, and safety of XEN45 implant, either alone or in combination with phacoemulsification surgery, in patients with glaucoma [11, 17, 22–24] (Table 5).

Regarding IOP lowering and reduction of glaucoma medication, the results of our study did not significantly differ from the currently available scientific evidence [11, 17, 22–24]. As far as we are concerned, there is only one study evaluating the efficacy and safety of XEN45 over a follow-up period of 4-years [11]. Lenzhofer et al. [11] reported a mean IOP lowering of 40.4% and a mean reduction in the number of ocular hypotensive medications of 1.2 drugs. Although the reduction of the ocular hypotensive drugs was not significantly different than that observed in our study, their IOP lowering seemed to be greater. Interestingly, we did not find significant differences in success rates.

Although the success rates observed in our study may not seem particularly high, it is important to note that the long-term rates of failure after trabeculectomy have been reported to be as high as 50% at 5 years [25, 26]. Regarding the MMC, in our study all the surgical procedures were performed with a MMC dose of 0.1%. Although the use of MMC may increase the success rate after XEN45 procedure, there is no agreement about the best MMC dose [27]. It has been recently published a paper comparing the efficacy and safety of XEN45 implanted with MMC 0.01% versus XEN45 implanted with MMC 0.02% [28]. They reported that MMC dose did not significantly influence either the IOP lowering or the reduction in the number of ocular hypotensive medication or the safety profile [28].

Different papers have evaluated the effectiveness of XEN in combination with phacoemulsification. There is not agreement regarding the superiority of the XEN alone over the XEN in combination with cataract surgery [7, 8, 10, 23].

Hengerer et al. [7] did not find significant differences in success rates between XEN and XEN+Phaco. Similarly, Karimi et al. [10] did not find significant differences in IOP lowering between XEN-alone and the XEN+Phaco groups. However, Mansouri et al. [8] and Gillman et al. [23] found higher success rates in the XEN-alone group.

Our study did not find significant differences in the success rates between XEN-alone and XEN+Phaco groups, although the postoperative IOP at day 1, week 1, and month 1 was significantly lower in the XEN-alone than in the XEN+Phaco group. These findings are in line with those reported by a meta-analysis published this year, which found a statistically significant difference in IOP reduction favoring Standalone XEN45 at postoperative day 1, week 1, month 1 [29]. According to the results of this metanalysis, XEN45 alone has superior IOP-lowering outcomes than XEN+Phaco, up to 6 months after surgery [29]. However, we did not find differences in IOP at months 3 and 6 between both groups.

As regards to the safety profile, the incidence and type of complications was similar to that previously published [5, 11, 17, 22–24, 29, 30]. However, we found a greater incidence of AEs at postoperative day 1 in the XEX+-Phaco group, but not in subsequent visits.

In our study, throughout the follow-up period, 82 (39.8%) eyes underwent some type of surgical procedure. The largest part of postoperative interventions was surgical revision of the conjunctival bleb, the rate of which was 17.5% (12.2%–24.2%). The rate of needling was 7.3% (4.1%–12.0%), with a mean time for needling 202.5 ± 172.3 days.

We did not find differences between groups either the rate of needling or the time for needling procedure, although the incidence rate of bleb revisions was significantly greater in the XEN+Phaco group. Several limitations should be taken into consideration when interpreting the results of the current study. The most important one is its retrospective design. Selection bias and potential confounders are inherent to retrospective studies. Nevertheless, the selection of strict inclusion/exclusion criteria, as well as the inclusion of a large number of eyes, may minimized these issues.

Conclusion

The results of this study suggest certainly that XEN implant, either alone or in combination with phacoemulsification, was able to significantly lowered the IOP and reduced the need of ocular hypotensive medication in the long-term. We found higher IOP reductions in the XEN solo group than in the XEN+Phaco one. However, they were only evident during the first month after surgery. Additionally, combined surgery was associated with a greater incidence of AEs at postoperative day 1 and a higher rate of bleb revisions.

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Statement of Ethics

The study protocol was approved by the Ethic Committee of the Miguel Servet University Hospital (Protocol number: 23/2021). The need for informed consent was waived by the Ethic Committee of the Miguel Servet University Hospital.

Any information that could lead to an individual being identified has been encrypted or removed, as appropriate, to guarantee their anonymity. The study protocol adhered to the tenets of the Declaration of Helsinki and the Good Clinical Practice/International Council for Harmonization Guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M.P.B. participated in the design, review, and coordination of the study. A.T., M.J.V., V.M., A.B.-M., and J.Y. participated in the collection of the data. C.I., B.F., E.F., S.P.-O., and N.G. participated in the design and analysis of the data. J.M.L., V.P., and L.E.P. participated in the analysis if the results and the correction of the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author (M.P.B.), upon reasonable request.

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