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Effectiveness of MicroShunt in Patients with Primary Open-Angle and Pseudoexfoliative Glaucoma

A Retrospective European Multicenter Study

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Purpose: To evaluate the effectiveness and safety of the Preserflo MicroShunt implant (Santen) in patients with primary open-angle glaucoma (POAG) and pseudoexfoliation glaucoma (PXG).

Design: Retrospective, open-label, multicenter study.

Participants: Patients with insufficiently controlled primary POAG or PXG who underwent a standalone MicroShunt implantation procedure.

Methods: Consecutive patients with POAG and PXG who underwent surgery with the ab externo minimally invasive glaucoma surgery device Preserflo MicroShunt with mitomycin C.

Main Outcome Measures: Primary end points were mean change in intraocular pressure (IOP) and number of hypotensive medications from baseline through month 12. Success was defined as an IOP of 18 mmHg or less and an IOP reduction of 20% or more, with (qualified) or without (complete) any hypotensive medication.

Results: Among the 130 patients who underwent MicroShunt implantation, 104 fulfilled the inclusion and exclusion criteria and were included in the analysis. Eighty-one eyes (77.9%) were diagnosed with POAG and 23 eyes (22.1%) were diagnosed with PXG. The mean age was 71.4 $\pm$ 12.6 years, and 45 patients (43.3%) were women. Mean IOP was lowered significantly from 25.1 $\pm$ 6.5 mmHg at baseline to 14.1 $\pm$ 3.4 mmHg at month 12 ($P < 0.0001$). At month 12, 27 eyes (26.0%) were categorized as complete successes and 61 eyes (58.7%) were categorized as qualified successes. The mean number of hypotensive medications was reduced significantly from 3.0 $\pm$ 1.0 medications at the preoperative visit to 0.77 $\pm$ 0.95 medication at month 12 ($P < 0.001$). Throughout the study, 19 eyes (18.3%) required needling and 14 eyes (13.5%) underwent surgical revision. Eight eyes (7.7%) showed hyphema and 5 eyes (4.8%) showed choroidal detachment. These were resolved with medical therapy without sequelae. Four patients underwent subsequent surgeries, and 2 patients underwent trabeculectomy (at months 3 and 6): One patient underwent transscleral cyclophotocoagulation at month 3 and 1 patient underwent MicroPulse cyclophotocoagulation at month 4.

Conclusions: In this retrospective study, the MicroShunt effectively lowered IOP and the need for IOP-lowering medications. *Ophthalmology Glaucoma 2022;5:210-218 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Glaucoma is a sight-threatening condition that, in advanced stages, significantly impacts a patient's quality of life.[1–3] Many different treatment options, mainly focused on lowering intraocular pressure (IOP), are currently available for addressing its therapeutic management.[4] Although traditional glaucoma filtering surgery and drainage devices are very effective for IOP lowering,[5] they may be associated with severe complications, potentially leading to visual impairment.[6]

Minimally invasive glaucoma surgery comprises a series of different devices and procedures that modulate aqueous humor outflow facility via 1 of several routes.[7] Minimally invasive glaucoma surgery devices can target different aqueous humor outflow pathways, including via Schlemm's canal, via the suprachoroidal space, or via the subconjunctival space.[7] The subconjunctival space is the traditional outflow pathway for glaucoma drainage surgery. The Preserflo MicroShunt (Santen, Osaka, Japan), formerly known as the InnFocus MicroShunt (Santen formerly InnFocus, Miami, FL), is implanted ab externo and has been designed for treating patients with early to advanced open-angle glaucoma.[8]

The MicroShunt is a tube composed of poly(styrene-block-isobutylene-block-styrene), a biostable thermoplastic elastomer that has demonstrated biocompatibility and long-term stability.[9] Poly(styrene-block-isobutylene-block-styrene) has

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been associated with minimal inflammation or encapsulation, especially when compared with other implant materials, such as silicone rubber.[10] The currently available device is an 8.5-mm long poly(styrene-block-isobutylene-block-styrene) tube with an outer diameter of 350 μm and a lumen diameter of 70 μm.[10] This device has a 1.1-mm wingspan "fin" located approximately halfway down the tube to prevent leakage around the tube and to fix the tube to the sclera.[8,10] Few studies have evaluated the MicroShunt in a clinical trial setting,[11–17] and just 1 study investigated its effectiveness in a clinical setting.[16] The purpose of the current study was to evaluate the effectiveness and safety of the Preserflo MicroShunt in patients with open-angle glaucoma.

Methods

Design

This retrospective, open-label, multicenter study was conducted in 6 third-level European centers (4 in Italy, 1 in Sweden, and 1 in the United Kingdom). The study protocol was approved by the ethics committee of each participating center (Struttura Complessa Oculistica, Città Della Salute e Della Scienza di Torino, Dipartimento di Scienze Chirurgiche - Università Degli Studi di Torino, Torino, Italy; Ospedale S. Orsola, Ospedale di San Marino e Studio d'Azeglio, Bologna, Italy; U.O.C. Oculistica, Ospedale di Sassuolo, Sassuolo (MO), Italy; Department of Clinical Neuroscience, Division of Ophthalmology and Vision, Karolinska Institutet, Stockholm, Sweden; University Eye Clinic, San Giuseppe Hospital, IRCCS Multimedica, Milan, Italy; Manchester Royal Eye Hospital, UK) which waived the need for informed consent for conducting the study. Nevertheless, written informed consent was provided by all the participants before surgery. This study complied with the Good Clinical Practice/International Council for Harmonisation Guidelines, the tenets of the Declaration of Helsinki, and all applicable country-specific regulations governing clinical research, depending on which provided greater protection to the individual.

Study Participants

Consecutive patients with insufficiently controlled primary open-angle glaucoma (POAG) or pseudoexfoliative glaucoma (PXG), poor treatment adherence, or intolerance to topical hypotensive medication and who underwent a standalone MicroShunt implantation procedure were included in the study. Patients with any form of glaucoma other than POAG or PXG or cataract requiring surgical intervention were excluded from the analysis. Additionally, patients with pemphigoid, phacodonesis, or conjunctival scarring that could compromise the procedure outcomes in the surgeon's opinion also were excluded. Patients were instructed to withdraw topical and systemic ocular hypotensive medications on the day of surgery.

Surgical Technique

The Preserflo MicroShunt (Santen formerly InnFocus) was provided in a sterile packaged kit containing a 3-mm scleral marker, a 1-mm triangular-blade knife, 3 LASIK Shields (EYETEC), a marker pen, and a 25-gauge needle. All procedures were performed under local anesthesia by an experienced surgeon (A.M.F., G.L.L., E.M., M.E., M.S., and L.A.) (1 surgeon per center).

After removing the sterile package, the MicroShunt was rinsed with balanced sterile saline solution. After skin disinfection, a conjunctival peritomy was performed approximately 3 to 4 mm in length between the superior rectus muscles and either the medial or lateral rectus. After Tenon's capsule was dissected, a deep pocket was created using blunt scissors between the rectus muscles to approximately the equator. Bipolar cautery was used to achieve light hemostasis, as needed. Topical mitomycin C (MMC) (0.2−0.5 mg/ml) was placed into the subconjunctival space using 3 LASIK Shields for 2 to 3 minutes (MMC concentration and exposure times were decided based on the surgeon's preference and patient characteristics). After marking the sclera 3 mm from the limbus with the scleral marker, a 1-mm wide, 1- to 2-mm long shallow scleral pocket was made 3 mm posterior to and toward the limbus with a triangular-bladed knife. A 25-gauge needle then was passed through the scleral pocket into the anterior chamber, remaining parallel to the iris plane to decrease the risk of corneal endothelial cell loss, and then retracted, thereby creating a dissected tunnel. The MicroShunt was threaded bevel-up through the needle tunnel with forceps, and the 1.1-mm wingspan planar fins of the device were wedged into the 1-mm scleral pocket. A 23-gauge thin-wall cannula was used for flushing the MicroShunt from the distal end of the tube. The aqueous humor flow through the MicroShunt lumen was confirmed visually by the formation of a droplet on the distal tip of the device. The distal end of the device then was tucked beneath the conjunctiva and Tenon's capsule, followed by separate closure of the conjunctiva and Tenon's layer with 8-0 Vicryl or with 10-0 nylon sutures. The site was checked for bleb leaks.

Reintroduction of glaucoma medications, revision (including needling), digital ocular compression, anterior chamber reformation, or other reoperations were performed per surgeon discretion. After surgery, needling was performed according to the surgeon's preference. Surgeon criteria for needling included IOP increase over target, flat or fibrotic bleb, or high risk of bleb failure. Other bleb procedures, such as subconjunctival injections of MMC, 5-fluorouracil, or dexamethasone, were allowed during the follow-up. Before reintroducing hypotensive medication, surgeons performed either needling or revision first. They restarted topical therapy if, according to the surgeon's opinion, this was not adequate or if the patient declined to undergo these procedures.

Study Visits

The study protocol included a baseline visit (performed within 1 month before surgery) and 7 postoperative visits. Follow-up visits were performed at day 1, day 7 (± 1 day), and months 1, 3, 6, 9, and 12 (± 15 days). At baseline, collected information included demographic characteristics, IOP, best-corrected visual acuity (BCVA), slit-lamp examination of the anterior segment, dilated funduscopic examination, and computerized visual field assessment (24-2 Swedish Interactive Threshold Algorithm Standard strategy [Carl Zeiss Meditec]) if the patient had no previous visual field testing within 3 months from the baseline visit.

Follow-up visits included a complete anterior segment and bleb examination and IOP measurement. Dilated funduscopy was performed on the first postoperative day or whenever deemed necessary. Best-corrected visual acuity was measured at baseline and at the last follow-up visit (12 months). In the presence of wound dehiscence, frank hypotony, or clinical signs of hypotony, fluorescein strips were used to assess for Seidel's sign and a dilated examination was performed.

Definitions

Complete success was defined as an IOP of 18 mmHg or less, and an IOP reduction of 20% or more, without any hypotensive medication at the month 12 visit. Qualified success was defined as an IOP of 18 mmHg or more and an IOP reduction of 20% or more with topical hypotensive medication at the month 12 visit. In patients with an IOP of less than 4 mmHg for more than 2

consecutive visits, those who needed further glaucoma surgery, or those who underwent surgery for complications, treatment also was considered a failure. Surgery revision was considered a failure, although according to the guidelines received during training, some surgeons were advised to proceed to revision instead of needling.

Outcomes

The primary end points were the mean change in IOP and the number of hypotensive medications from baseline to month 12. Secondary end points included the proportion of patients achieving a month 12 IOP of 21 mmHg or less, an IOP of 18 mmHg or less, an IOP of 16 mmHg or less, and an IOP of 14 mmHg or less, regardless of the percentage reduction. The safety analysis included the incidence of adverse events, the proportion of patients with a BCVA reduction of 2 lines or more, and the need for needling or revisions.

Statistical Analysis

Statistical analysis was performed with Prism 9 version 9.0 software (GraphPad Software) and MedCalc Statistical Software version 19.6 (MedCalc Software, Ltd). Although the sample size was not calculated before the study, we conducted a post hoc power analysis to evaluate the adequacy of the sample. The post hoc power analysis was determined for an α level of 0.05, the study sample size, and the effect size observed in the study.[18] Patients with more than 30% missing data were dropped, and case-wise deletion was used in the remaining data set. Data were tested for normal distribution using a Shapiro-Wilk test. Variables with a normal distribution were expressed as mean ± standard deviation and were compared using repeated measures analyses of variance and the Greenhouse-Geisser correction test. Categorical variables were expressed as numbers (percentages) and were compared with a Fisher exact test or chi-square test as appropriate. A P value of < 0.05 was considered significant, and all tests were 2-tailed.

Results

Among the 130 patients who underwent MicroShunt implantation, 26 were excluded from the analysis. Eighteen patients had undergone combined surgery (MicroShunt plus phacoemulsification), and 8 patients had a clinical diagnosis other than POAG or PXG (1 with juvenile glaucoma, 4 with primary angle-closure glaucoma, and 3 with uveitic glaucoma). A total of 104 eyes from 104 patients met all the inclusion and exclusion criteria and were included in the analysis.

Data for 3 eyes at month 12 were not available because of revisions in the same period. Of the 104 patients, data were available for 104 at day 1, 103 at week 1 and month 1, 101 at month 3, 89 at month 6, 85 at month 9, and 94 at month 12. In some patients, observed follow-up time was less than the length of the study because they did not reach the study timeline, and not because of early withdrawal.

No significant differences were found in IOP ($P = 0.16$), the number of ocular hypotensive medications ($P = 0.24$), visual field parameters (mean defect, $P = 0.26$; and pattern standard deviation, $P = 0.22$), or BCVA ($P = 0.64$) among the different study centers at baseline. The mean age was 71.4 ± 12.6 years, and 45 patients (43.3%) were women. Eighty-one eyes (77.9%) had a clinical diagnosis of POAG, and 23 eyes (22.1%) had a clinical diagnosis of PXG. The main demographic and clinical characteristics are shown in Table 1.

Table 1. Main Demographic and Clinical Characteristics of the Study Population (N = 104 Eyes)

Variable	Data
Age, yrs	71.4 ± 12.6
White race	104 (100.0)
Sex	
Women	45 (43.3)
Men	59 (56.7)
Eye	
Right	53
Left	51
Functional	
One-eyed	23 (21.3)
Two-eyed	81 (78.7)
Lens status	
Phakic	46 (44.7)
Pseudophakic	56 (54.4)
Missing information	2 (1.9)
Glaucoma type	
Primary open-angle glaucoma	81 (77.9)
Exfoliative glaucoma	23 (22.1)
Previous laser treatment	
None	73 (70.2)
ALT	1 (0.9)
SLT	30 (28.9)
Previous surgery	
None	88 (84.6)
Trabeculectomy	4 (3.8)
XEN	3 (2.9)
Schlemm's canal surgery (Hydrus)	3 (2.9)
Deep sclerectomy	1 (1.0)
CyPass	1 (1.0)
High-intensity ultrasound cyclocoagulation	1 (1.0)
Vitrectomy (epiretinal membrane)	2 (1.9)
PKP	1 (1.0)
SCAI	
Yes	49 (47.1)
No	55 (52.9)
Preoperative IOP, mmHg	25.1 ± 6.5
Preoperative medications	3.0 ± 1.0
Central corneal thickness, µm	527.6 ± 28.8
Visual field, dB	
Mean defect	−10.7 ± 7.7
Pattern SD	7.6 ± 3.4
BCDVA	0.61 ± 0.3

ALT = argon laser trabeculoplasty; BCDVA = best-corrected distance visual acuity; PKP = penetrating keratoplasty; SCAI = systemic carbonic anhydrase inhibitors; SD = standard deviation; SLT = selective laser trabeculoplasty.
Data are presented as mean ± standard deviation or no. (%).

Efficacy

As compared with preoperative IOP, mean IOP lowering was −16.6 mmHg (95% CI, −14.9 to −18.3 mmHg), −14.8 mmHg (95% CI, −12.9 to −16.7 mmHg), −11.32 mmHg (95% CI, −9.3 to −13.3 mmHg), −11.2 mmHg (95% CI, −9.4 to −13 mmHg), −10.2 (95% CI, −8.5 to −11.91 mmHg), −10.5 mmHg (95% CI, −9 to −13 mmHg), and −10.1 mmHg (95% CI, −8.5 to −11.8 mmHg) at day 1, week 1, month 1, month 3, month 6, month 9, and month 12, respectively ($P < 0.0001$ for each; Fig 1). Data were plotted from baseline IOP on the x-axis and from last follow-up visit IOP on the y-axis to make an overall visual assessment (Fig 2). As compared with

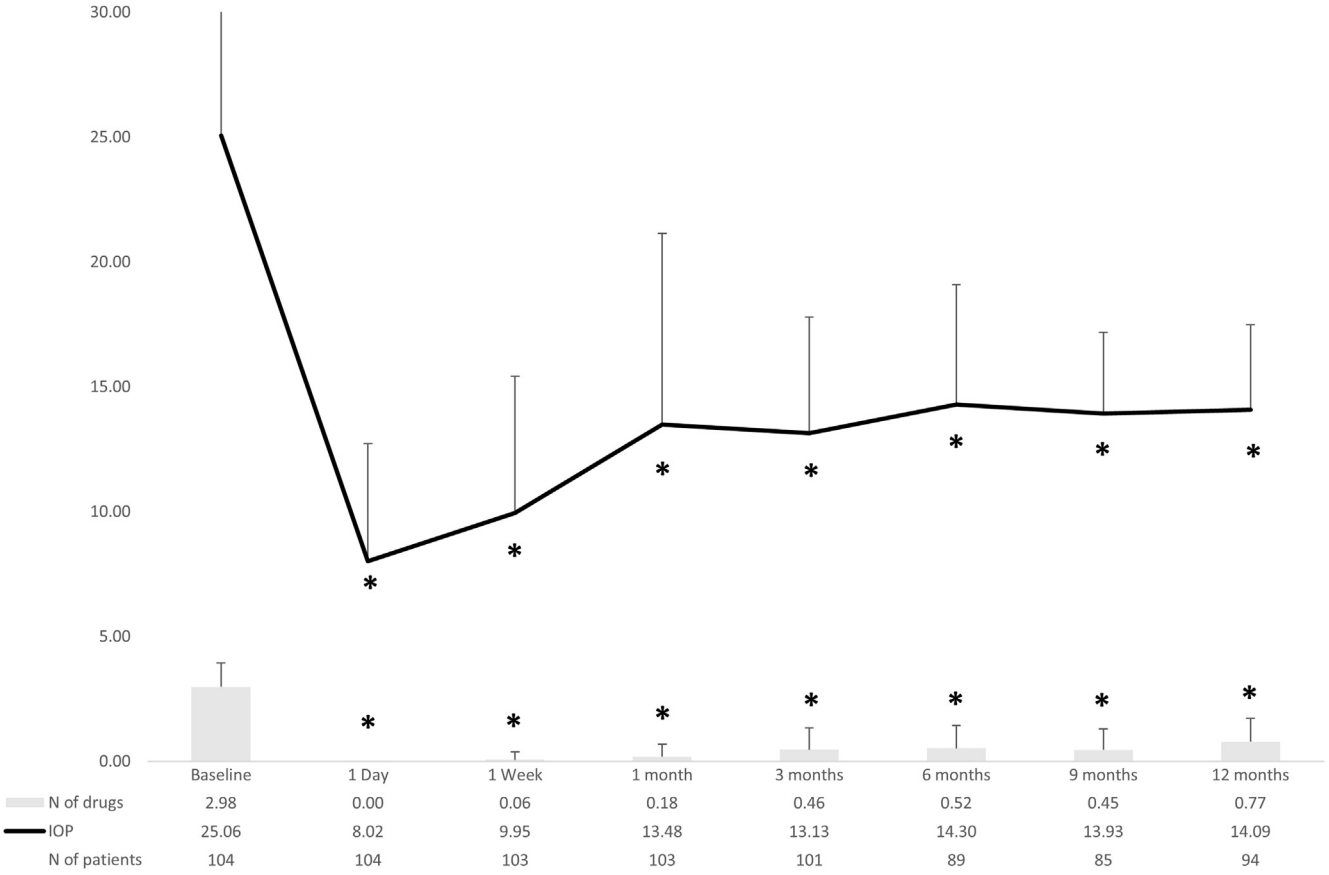

Figure 1. Graph showing mean intraocular pressure (IOP) and mean number of hypotensive treatments in the overall study sample. The vertical bars represent the 95% confidence interval. *$P < 0.0001$ compared with baseline (repeated measures analysis of variance and the Greenhouse-Geisser correction).

baseline, all but 4 patients had either equal or a lower IOP at month 12, with many of them achieving an IOP reduction of 20% or more (79/94 eyes) and 30% or more (66/94 eyes). At month 12, 27 eyes (26.0%) were categorized as complete success and 61 eyes (58.7%) were categorized as qualified success. Table 2 shows the proportion of eyes that achieved different IOP targets regardless of the percentage reduction from baseline.

In eyes with POAG, mean IOP dropped significantly from 25.0 ± 6.7 mmHg at baseline to 14.3 ± 3.6 mmHg at month 12 (mean difference, −10.7 ± 5.5 mmHg; 95% CI, −12.5 to −8.9 mmHg; $P < 0.0001$). Regarding eyes with PXG, preoperative IOP was lowered significantly from 25.0 ± 5.9 mmHg to 13.5 ± 2.4 at month 12 (mean difference, −11.5 ± 4.5 mmHg; 95% CI, −14.2 to −8.8 mmHg; $P < 0.0001$). We did not find significant differences when comparing the mean IOP-lowering effect between POAG and PXG eyes at month 12 ($P = 0.5244$).

In the overall study sample, the mean number of hypotensive medications was reduced significantly from 3.0 ± 1.0 drugs at the preoperative visit to 0.8 ± 1.0 drugs at month 12 ($P < 0.0001$). In eyes with POAG, the number of ocular hypotensive medications was reduced significantly from 2.9 ± 1.0 at baseline to 0.8 ± 0.9 at month 12 ($P < 0.0001$). Similarly, a significant reduction ($P < 0.0001$) was observed in the number of hypotensive medications in the PXG group from baseline (3.0 ± 1.0) to month 12 (0.8 ± 1.0), with no significant differences between POAG and PXG eyes ($P = 0.9616$).

No significant differences were found in terms of month 12 IOP ($P = 0.23$), delta IOP ($P = 0.26$; the difference between month 12 IOP versus baseline IOP), month 12 number of ocular hypotensive medications ($P = 0.75$), and delta ocular hypotensive medications ($P = 0.61$) between phakic and pseudophakic eyes. Our study did not find any difference in terms of IOP reduction among the different study centers at month 12 (both absolute value and percentage value; *P* value ranged from 0.6625 to >0.9999 and from 0.9468 to >0.9999, respectively, Tukey's multiple comparisons test).

Safety

The incidence of adverse events is summarized in Table 3. The most common adverse event was hyphema (8 eyes [7.7%]) and choroidal detachment (5 eyes [4.8%]). All the adverse events were mild in severity and resolved successfully with medical treatment. No sight-threatening complications were observed.

Needling was performed in 19 eyes (18.3%) and surgical revision was performed in 14 eyes (13.5%). Four eyes (3.9%) underwent both procedures, first needling and later a revision. The median time between surgery and first needling was 30.0 days (interquartile range, 30.0−60.0 days), whereas the time between

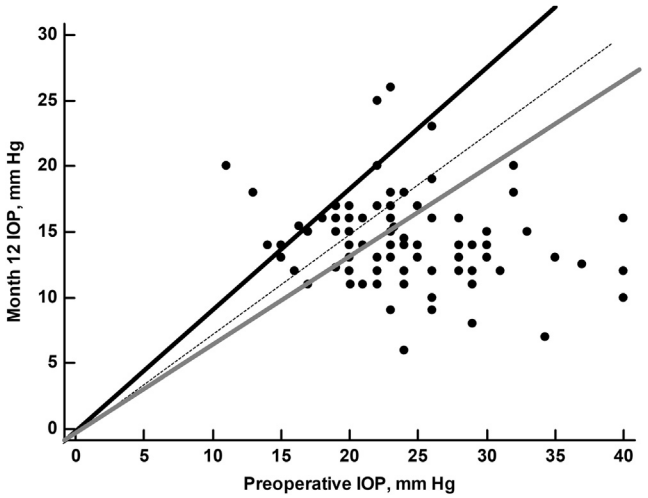

Figure 2. Scatterplot showing the preoperative intraocular pressure (IOP) and month 12. Mean difference, −10.4 mmHg; 95 confidence interval, −12.0 to −8.8 mmHg; $P < 0.0001$ (2-tailed paired-samples Student t test). Dotted black line represents 20% IOP lowering. Solid grey line represents 30% IOP lowering.

surgery and surgical revision was 60.0 days (interquartile range, 30.0−180.0 days). Compared with eyes that did not undergo needling or surgical revision, no significant differences were found in age versus those who underwent needling ($P = 0.6196$) or those who underwent surgical revision ($P = 0.8211$).

Regarding other procedures, 9 eyes (8.7%) received digital ocular massage, and 5 eyes (4.8%) and 3 eyes (2.9%) underwent postoperative subconjunctival injections with MMC and 5-fluorouracil (without needling), respectively. Because some patients underwent multiple needling or revision interventions, the total number of interventions was 29 needling and 14 revision procedures. Four patients underwent subsequent surgeries: 2 underwent trabeculectomy (at months 3 and 6), 1 underwent transscleral cyclophotocoagulation at month 3, and 1 underwent MicroPulse cyclophotocoagulation at month 4; the data after these treatments were not included in the analysis, and treatment was considered to have failed in these patients.

Nine patients experienced a reduction in BCVA of more than 2 lines, 8 patients because of cataract progression and 1 patient because of worsening macular edema. One diabetic patient with macular edema received an injection of a vascular endothelial growth factor inhibitor at the time of MicroShunt surgery and a subsequent injection at month 7.

Table 2. Overview of the Proportion of Patients Who Achieved Specific Intraocular Pressure Levels, with and without Hypotensive Medication, at Month 12

Intraocular Pressure (mmHg)	Month 12 (n = 94), No. (%)			
	With Treatment		Without Treatment	
≤ 12	34	36.2	24	25.5
≤ 14	57	60.6	39	41.5
≤ 16	76	80.1	51	54.3
≤ 18	87	92.6	55	58.5
≤ 21	91	96.8	55	58.5

Table 3. Adverse Events Observed or Reported during the Study Follow-up

Adverse Event	No. (%)
Hyphema	8 (7.7)
Choroidal detachment	5 (4.8)
Hyphema with hematic Tyndall	2 (1.9)
Device captured in Tenon's capsule	1 (1.0)
Choroidal hemorrhage	1 (1.0)
Blood clot blocking the lumen	1 (1.0)
Hypertrophic bleb with corneal dellen	1 (1.0)

Discussion

Medical therapy is the most common approach to glaucoma treatment; however, rates of medication adherence and persistence with glaucoma medications are low,[19,20] which may impact clinical outcomes significantly.[21] In patients whose glaucoma is not controlled adequately with medication, surgery represents a valuable strategy.[4,5] According to the results of this study, the MicroShunt was effective for lowering IOP and reducing the number of hypotensive medications in patients with open-angle glaucoma for 12 months. Additionally, a proportion of patients achieved low target IOPs: 21.5% and 41.5% of patients achieved an IOP of less than 12 mmHg and less than 14 mmHg without treatment, respectively.

Trabeculectomy and drainage device insertion are commonly performed incisional glaucoma surgeries.[22] Despite their good IOP-lowering effectiveness, they are associated with a relatively high incidence of early and late postoperative interventions and complications.[6,22,23] Therefore, the need exists to develop safer surgical techniques that maintain efficacy in terms of IOP lowering. Among the other minimally invasive glaucoma surgeries currently available in the market is insertion of the MicroShunt, an ab externo and subconjunctival minimally invasive glaucoma surgery device with a good efficacy and safety profile.[11−17]

The results of a head-to-head study comparing MicroShunt (implanted alone) versus trabeculectomy found no differences in terms of IOP lowering between them (at month 12, mean IOP dropped from 21.1 ± 4.9 mmHg to 14.2 ± 4.4 mmHg and from 21.1 ± 5.0 mmHg to 11.2 ± 4.2 mmHg in the MicroShunt and trabeculectomy groups, respectively). The number of ocular hypotensive drugs was reduced significantly from 3.0 at baseline to 0.6 in the MicroShunt group and to 0.3 in the trabeculectomy group at month 12.[24]

However, the results of another head-to-head prospective, randomized study that compared the effectiveness and safety of standalone MicroShunt implantation versus trabeculectomy in patients with POAG found lower success rates, higher mean IOP, and more ocular hypotensive medications in the MicroShunt group over 1 year.[17] Interestingly, fewer patients required postoperative interventions after MicroShunt implantation compared with those who underwent trabeculectomy, which meant

Table 4. Overview of the Intraocular Pressure and Number of Hypotensive Medications in Eyes That Underwent MicroShunt Implant Surgery in Different Studies

Study	Intraocular Pressure (mmHg)		Intraocular Pressure Lowering		Medications		Success Rates (%)	
	Baseline	*Month 12*	*Percentage*	*Millimeters of Mercury*	*Preoperative*	*Postoperative*	*Qualified*	*Complete*
Riss et al[11]								
MMC 0.4 near limbus	23.8 ± 5.3	10.7 ± 2.8	−55.0*	NP	2.4 ± 0.9	0.3 ± 0.8	NP	NP
MMC 0.2 near limbus	27.9 ± 4.7	13.3 ± 3.3	−52.0*	NP	2.5 ± 1.4	0.5 ± 1.0	NP	NP
MMC 0.4 far limbus	25.4 ± 7.9	15.7 ± 4.6	−38.0*	NP	2.9 ± 1.0	0.8 ± 1.3	NP	NP
Batlle et al[12]	23.8 ± 5.3	10.7 ± 2.8	−55.0*	NP	2.4 ± 0.9	0.3 ± 0.8	100.0	91.0
Scheres et al[13]	20.1 ± 5.0	12.1 ± 3.5	−40.0*	NP	2.3 ± 1.5	0.6 ± 1.0	79.0	58.0
Beckers et al[15,†]	21.9 ± 3.7	13.5 ± 3.1	NP	NP	2.0 ± 1.3	0.1 ± 0.4	74.4[‡]	
Schlenker et al[16]	20.0 (16.5–26.0)[§]	12.0 (10.0–15.0)[§]	NP	NP	4.0 (3.0–4.0)[§]	0.0 (0.0–0.0)[§]	92.5	72.9
Baker et al[17]	21.1 ± 4.9	14.3 ± 4.3	−29.1*	−6.5	3.1 ± 1.0	0.6 ± 1.1	53.9[‡]	
INN-005[23]	21.9 ± 4.9	14.2 ± 4.4	NP	NP	3.0*	0.6*	NP	NP
Current study	25.1 ± 6.5	14.1 ± 3.4	−59.7	−10.4 (−12.0 to −8.8)[‖]	3.0 ± 1.0	0.8 ± 1.0	58.7	26.0

NP = not provided.
*Data about standard deviation was not provided.
†Data at year 2.
‡The article does not specify whether success was complete or qualified.
§Median (interquartile range).
‖Mean (95% confidence interval).

less frequent postoperative visits and therefore a presumed cost savings.[17]

When comparing our results with the current evidence, the IOP-lowering effect seemed to be slightly lower than that reported by Riss et al,[11] Batlle et al,[12] Batlle et al,[14] or Schlenker et al,[16] but similar to that found by Beckers et al,[15] the INN-005 (a prospective, randomized, controlled, single-masked, multicenter study to assess the safety and effectiveness of DE-128 [MicroShunt] standalone, without concomitant cataract extraction),[24] or that observed by Baker et al[17] (see Table 4). In fact, taking into consideration the articles published recently, the month 12 IOP and the reduction of ocular hypotensive medications were quite similar.[15,17,24] The final postoperative IOP observed in our study, on average, was a little higher than that predicted Kudsieh et al[25] for eyes with a preoperative IOP of 25 mmHg, although the mean preoperative IOP found in our study was very close to it. Regarding success, except for the qualified success rate reported by Scheres et al,[13] which was similar to ours, both complete and qualified success rates found in our study were, on average, lower than those reported by others.[12–17] Differences in study protocols, concentration and placement of MMC, and the fact that the current study was conducted in a clinical setting may justify such differences.

As shown in Table 4, the mean preoperative IOP of our sample was higher than that reported by others. Although lower preoperative IOP may hamper the achievement of a specific percentage reduction, higher preoperative IOP may be associated with lower surgical success rates.[16] Last but not least, limited experience with the device might have played a role in the results. Regarding the efficacy profile, depending on the type of glaucoma, the current study did not find significant differences between POAG and PXG in IOP lowering at month 12 ($P = 0.5244$).

Evidence suggests disruption of the blood–aqueous barrier in patients with PXG after intraocular surgery.[26,27] This blood–aqueous barrier breakdown may be an essential risk factor for early or late postoperative complications.[26] In our study, topical steroids therapy after MicroShunt implantation was neither more intensive nor more prolonged in PXG patients. This finding might suggest that the MicroShunt induces a lower inflammatory response, but further studies would be required to evaluate this subject. Similarly, no significant differences were observed in IOP and the number of glaucoma medications at month 12 or their changes from baseline, between phakic and pseudophakic eyes. Aphakic and pseudophakic eyes would be associated with an increase in inflammatory mediators because of blood–aqueous barrier breakdown,[28] which may lead to worse clinical outcomes after trabeculectomy.[29] However, the results of a 5-year retrospective study did not find significant differences in clinical outcomes between aphakic and pseudophakic eyes.[30]

Mitomycin C application times and dosage have been proposed as an essential element to the success of the surgical procedure.[12,14–17] In fact, higher MMC concentrations have been associated with a lower risk of MicroShunt failure.[16] In our study, IOP lowering was not related to MMC

concentration or exposure time. This fact may be the result of our study protocol, because the different strategies, both in dose (ranging between 0.2% and 0.5%) and in application time (ranging from 2 to 3 minutes) used by the surgeons who participated in the current retrospective study would not allow detection of any difference in IOP lowering. Because no clear consensus about the most efficacious dose and exposure of MMC during glaucoma surgery has been achieved,[31] further research is needed to clarify this subject.

From a clinical perspective, it should be mentioned that although this was the first time using the device for many surgeons, no differences were found in terms of IOP reduction among the different study centers, which suggests that the learning curve may be easily overcome. In addition to its good efficacy and safety profile, this fact might help to generalize the technique among glaucoma surgeons. Regarding safety, the incidence of adverse events did not differ significantly from those published previously.[14,16,17] The most frequent adverse event was hyphema, followed by choroidal detachment. Adverse events were mild in severity, and all resolved fully with medical treatment.

Needling was performed in 19 eyes (18.3%) and surgical revision was performed in 14 eyes (13.5%). The rate of needling was higher than that reported by Schlenker et al,[16] but in line with that reported by Baker et al.[17] It should be highlighted that in 10 patients (71.4%), surgical revision was performed as a primary procedure instead of needling because during training, some surgeons were instructed to perform surgical revisions, rather than needling.

The current study has some limitations that should be taken into account when interpreting its results. The first of these are its retrospective design and the lack of a control group. Confounding factors and bias are inherent to retrospective studies. To minimize this limitation, we conducted a multicenter study and selected strict inclusion and exclusion criteria. The second limitation was not calculating the sample size before starting the study.

Nevertheless, the power for detecting the observed differences in IOP lowering and reduction of hypotensive medication between preoperative values and month 12 was 99% each, respectively. Additionally, the sample size, the excellent rate of patients who remained in the study at month 12, and its multicenter design provided sufficient strength to the study. Another limitation is the lack of information about the impact of the MicroShunt on the corneal endothelium because endothelial cell loss was not evaluated. A strength of the study is that 10 eyes (9.6%) had undergone previous glaucoma surgery, which represents a challenge for MicroShunt results. Mean IOP and number of ocular hypotensive medications at month 12 were 14.2 $\pm$ 5.7 mmHg and 0.7 $\pm$ 0.8 drugs, respectively. Three eyes had undergone a previous XEN45 implantation. In these eyes, the mean IOP at month 12 was 13.0 $\pm$ 5.3 mmHg, with a mean IOP lowering from baseline of 15.0 $\pm$ 10.4 mmHg; no eyes required ocular hypotensive medication. Among the eyes that had undergone a previous glaucoma surgery, 1 eye underwent subsequent surgery (cyclophotocoagulation), 2 eyes required needling, and 3 eyes required revision.

In conclusion, according to the results of this study, the Preserflo MicroShunt is a safe and effective device for lowering IOP and the need for IOP-lowering medications, with a relatively high success rate. However, further investigation is needed to confirm this finding. Adverse events were transient, and no long-term sight-threatening adverse events were reported. Finally, because of the short-term follow-up and the small number of patients, we cannot provide sufficient evidence of the results of subsequent surgery after Preserflo MicroShunt implantation. Further research is needed to elucidate these issues.

Footnotes and Disclosures

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HUMAN SUBJECTS: Human subjects were included in this study. Study protocol was approved by the Ethics Committee of each of the participating centers, which waived the need of informed consent for conducting the study. Nevertheless, written informed consent was provided by all the participants before surgery. This study complied with the Good Clinical Practice/International Council for Harmonisation Guidelines, the Declaration of Helsinki, and all applicable country-specific regulations governing the conduct of clinical research, depending on which provided greater protection to the individual.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Fea

Analysis and interpretation: Fea, Laffi, Martini, Economou, Au

Data collection: Fea, Laffi, Martini, Economou, Caselgrandi, Sacchi, Au

Obtained funding: N/A

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Abbreviations and Acronyms:
ANOVA = analysis of variance; **BCVA** = best-corrected visual acuity; **CI** = confidence interval; **IOP** = intraocular pressure; **MMC** = mitomycin C; **POAG** = primary open-angle glaucoma; **PXG** = pseudoexfoliation glaucoma.

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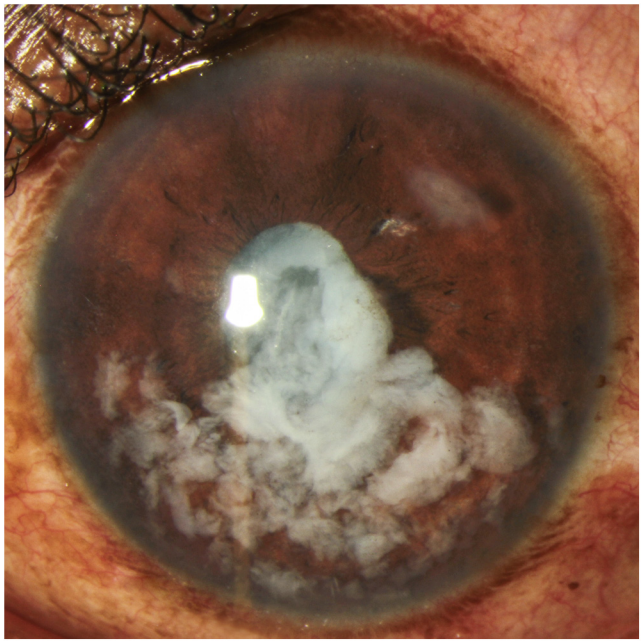
Pictures & Perspectives



Lens Particle Glaucoma after Penetrating Injury

Lens particle glaucoma results from liberated lens material after the lens capsule is compromised from cataract surgery or post-trauma. A middle-aged man with an alleged thorn injury 2 weeks previous in his left eye (LE) presented with pain, redness, and decreased visual acuity. Best-corrected visual acuity (BCVA) in LE was hand motions and intraocular pressure (IOP) was 42 mmHg. Ocular examination revealed self-sealed horizontal corneal tear of 2 mm paracentrally with a corresponding iris entry wound and floating lens particles in the anterior chamber (Fig 1). He was administered topical aqueous suppressants, steroids, and cycloplegics. Subsequently, he underwent cataract extraction with scleral-fixated intraocular lens. Postoperative BCVA and IOP was 6/24 and 20 mmHg, respectively (Magnified version of Fig 1 is available online at www.ophthalmologyglaucoma.org).

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