Original Article

Application of high intensity focused ultrasound for treatment of open-angle glaucoma in Indian patients

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Purpose: The aim of this study is to assess the efficacy of ultrasound cycloplasty (UCP) in Indian patients with open angle glaucoma (OAG). **Methods:** A prospective interventional study was designed to treat 73 eyes of 73 patients with OAG with the EyeOP1 device equipped with six miniaturized cylindrical piezoelectric transducers. Two treatment protocols of ultrasound delivery depending on exposure time (8 s and 10 s of shot per transducer) were used. Complete ophthalmic examination, ocular biometry and anterior segment optical coherence tomography were performed preoperatively and patients were followed up at day 1, day 7 and months 1, 2, 3, 6, and 12. The primary outcome measure was "successful" intraocular pressure (IOP) control defined as IOP reduction ≥20% from baseline and IOP value >5 mm Hg at the last follow-up visit. Secondary outcomes were the occurrence of complications and mean IOP during the follow-up period. **Results:** In all patients, the mean IOP reduced from 23.5 ± 3.0 mmHg before treatment to 15.7 ± 5.4 mmHg at 12 months ($P < 0.05$). Successful IOP control after a single procedure was 78.3% (79% and 78% in the 8 s and 10 s groups, respectively) at 12 months. Overall, the mean IOP reduction achieved in responding patients was 41% (standard deviation = 12%). Notwithstanding minor side effects such as transient pain, anterior chamber reaction, and refractive error changes, no major intraoperative or postoperative complications (severe hypotony or phthisis) were observed during the follow-up. **Conclusion:** Our short-term results reveal that UCP is a simple, safe, and noninvasive procedure which enables to significantly reduce the IOP in patients with OAG. The study results in Indian eyes corroborate findings in earlier studies on Caucasian eyes.

Key words: Cycloablation, glaucoma, ultrasound

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Glaucoma is the second major cause of blindness with an estimated 64 million cases worldwide which is likely to increase to 76 million by 2020 and 111 million by 2040.[1] In India, out of 12 million people affected, about 6.5 million people suffer from primary open angle glaucoma (POAG).[2] Reduction of intraocular pressure (IOP) has been shown to be the only treatable risk factor which can halt the progression of the disease.[3] This can be achieved either by (i) improving the outflow of aqueous humor by medications, laser, or incisional surgery and (ii) reducing the production of aqueous humor by medications or partial coagulation/destruction of the ciliary body. Medications are considered as first-line treatment and surgery reserved for advanced, resistant, and drug-intolerant cases. The coagulation techniques that reduce the production of aqueous humor employ various energy sources including laser, microwave, cryo and ultrasound.[4] However, they have two major drawbacks: (i) inability to focus the energy over a specific target organ, which results in collateral tissue damage, (II) unpredictable dose-effect relationship which prevents the titration of treatment effect.[5] Therefore, cyclodestruction is considered as an end-stage procedure when all other modalities fail, and its use is currently limited to treatment of refractive glaucoma in eyes with limited visual potential.

Laser treatment can be applied to the intact anterior sclera using continuous-wave red and diode near-infrared lasers (transscleral cyclophotocoagulation [CPC]), or it can be directly applied to the ciliary processes [endoscopic CPC] in an invasive manner using diode near-infrared continuous-wave laser energy. Diode laser CPC is the most commonly used ciliary ablation technique but associated with side effects such as chronic uveitis, hypotony, serous retinal detachment, and phthisis.[6,7] In this scenario, high intensity focused ultrasound (HIFU) has been proposed as a more controlled and predictable method of cycloablation, indicated not only in end-stage disease but also in refractory cases with useful vision. HIFU is used to trigger hyperthermia in focal areas in the ciliary body, thereby reducing aqueous production and IOP. One of the advantages of HIFU over diode laser is that the energy can be focused through optically opaque media on a target organ with controlled energy absorption and reduced adjacent tissue damage. The effect is independent of ciliary body pigmentation which can cause variation in energy deposition and tissue heating at focus site. HIFU can be used to treat a defined tissue volume at any depth or location

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within the eye enabling accurate dosing and prediction of treatment effect.[8] Ultrasonic coagulation of the ciliary body using HIFU was introduced in the 1980s but later discarded due to the increased incidence of complications attributed to the methodology and bulky transducer size.[9,10] In view of the recent advancements in ultrasound technology, a new HIFU device called EyeOP1 (Eye Tech Care, Rillieux-la-Pape, France) using miniaturized transducers was developed. After a series of successful clinical trials in Europe, this device has obtained European Conformity (CE) approval for treatment of refractory glaucoma and is commercially available. We conducted a prospective, open-label, interventional clinical study to evaluate the safety and efficacy of this device for the treatment of OAG in Indian patients.

Methods

This prospective clinical study was conducted in compliance with the Declaration of Helsinki and the standards of ISO 14155:2011: Clinical Investigations of Medical Devices for Human Subjects– Good Clinical Practices. The protocol followed the World Glaucoma Association guidelines on the design and reporting of glaucoma surgical trials.[11] The study was approved by an independent ethics committee and registered under the Clinical Trials Registry of India (CTRI/2014/04/006797). Written informed consent of each individual was obtained before enrolment in the study, and the consenting process was recorded.

High intensity focused ultrasound device

The EyeOP1 device comprises two functional elements, (1) a sterile single-use treatment pack, which includes a coupling cone and a treatment probe, and (2) a compact, lightweight operator console with built-in aspiration and ultrasound delivery components [Fig. 1]. A polymer coupling cone is placed over the eye centered at the limbus and is maintained in position using low-level vacuum generated in a suction ring located at the base of the cone. A ring-shaped treatment probe equipped with six active piezoelectric transducers is inserted in the upper portion of the coupling cone. The space created between the eye, the cone and the treatment probe is filled with sterile saline solution (BSS; Alcon Laboratories Inc., Fort Worth. TX, USA) to ensure propagation of ultrasound energy. The transducers, placed radially at regular intervals on the superior and inferior circumference of the probe avoiding the nasal and temporal meridian, are oriented to create a focal zone consisting of six regularly distributed elliptical impressions measuring 0.1 cm × 1 mm located 0.7 mm deep inside the ciliary body. The resonant frequency of the transducers is 7 MHz, and the device is operated at 21 MHz. Choice of three different probe diameters of 11 mm, 12 mm, and 13 mm is available for optimal target localization based on the subject's eye anatomy. Ocular biometry (anterior segment optical coherence tomography [OCT], axial length, and white-to-white measurement) is performed prior the procedure to determine the diameter to be used.

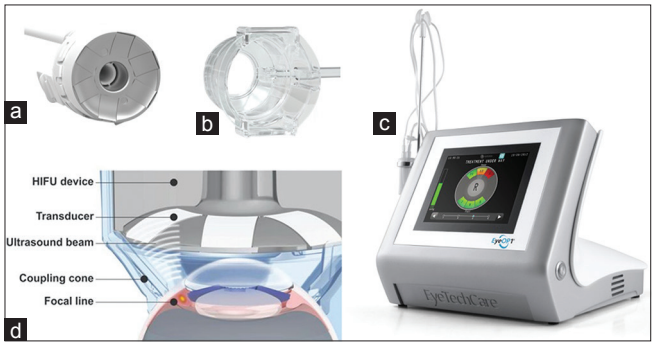

Figure 1: High intensity focused ultrasound device components. (a) Treatment probe with six miniaturized piezoceramic transducers. (b) Coupling cone. (c) Ultrasound console. (d) Cross-section of the high intensity focused ultrasound device and coupling cone placed on the eyeball maintained in position by a suction ring. The ultrasound beam generated from the transducer focuses on a linear area (dotted line) within the ciliary body

The treatment probe is connected to a control module by a cable, which conducts the electrical signal that generates the ultrasound beams. A touch-screen enabled computer screen allows the user to define the treatment conditions. All parameters including frequency, power, and number of transducers activated are fixed (predetermined), and only the duration of each shot per transducer can be defined by the operator (8 s or 10 s). The computer activates each transducer sequentially as per predefined software. In the present study, a second-generation probe that has an active transducer area of 4 mm compared to 2.5 mm in the first-generation probe was used. The other improvements in the second-generation probe included (1) optimized suction and centering of the cone over the eye, (2) improved ultrasound coupling by the elimination of air bubbles which could interfere with the ultrasound beam, and (3) enhanced ergonomics and an improved clip to fix the probe with the cone.

Patients

Before the initiation of this trial, a prospective pilot clinical study (ETC-IND-01) was conducted to evaluate the safety of the EyeOP1 device. Fifteen individuals diagnosed with either primary or secondary glaucoma and having no vision potential were enrolled and treated with the second-generation probe. The primary safety end-point for the study was the incidence of any device or procedure-related adverse events, and patients were followed up for 3 months. In the absence of any adverse effects in the pilot study, the main prospective interventional clinical study (ETC-IND-02) was conducted.

Inclusion criteria were as follows: (1) diagnosis of POAG, pseudoexfoliative or pigmentary glaucoma with or without prior trabeculectomy, (2) average baseline IOP between ≥21 mm Hg and ≤45 mm Hg not adequately controlled with glaucoma medications, (3) age between 18 and 90 years, and (4) no previous intraocular surgery or laser treatment during the 90 days before procedure. Exclusion criteria were as follows: (1) angle-closure glaucoma or narrow anatomical anterior chamber (Shaffer Grade 0/1), (2) normal tension glaucoma, secondary glaucoma and aphakia, (3) history of cyclo-destructive procedure or glaucoma drainage device implantation, (4) any ocular or retrobulbar tumor or ocular infection within past 2 weeks, and (5) ocular disease other than glaucoma that may affect assessment of visual acuity and/or IOP (choroidal hemorrhage/detachment, lens subluxation, proliferative diabetic retinopathy, clinically significant macular edema).

Procedure

Seventy-three patients with OAG, who met the above inclusion criteria, were enrolled for treatment. Baseline evaluation included best corrected visual acuity (BCVA), slit lamp biomicroscopy with gonioscopy using four mirror goniolens

on the handle, IOP measurement by Goldmann applanation tonometry (3 measurements) and dilated fundus examination by + 90D lens and indirect ophthalmoscopy. Preoperative investigations included axial length and white-to-white measurements by IOLMaster 500 (Carl Zeiss Meditec AG., Jena, Germany), corneal topography by Orbscan IIz Corneal Analysis System (Bausch and Lomb Inc. Bridgewater, NJ), ultrasound pachymetry with Tomey SP-100 (Tomey Corp. Nagoya, Japan), visual fields using Humphrey Field Analyzer 24-2 SITA Standard programme (Carl Zeiss Meditec AG., Jena, Germany) and transverse quad scans of anterior segment with Visante™ AS-OCT (Carl Zeiss Meditec AG., Jena, Germany). To determine the appropriate probe size, a proprietary computer-assisted overlay drawing software was used, wherein the anterior OCT images were superimposed onto the probe model whose focal zones matched the ciliary body and the model (coupling cone and probe) that best targeted the ciliary body was chosen.

Based on the exposure time of each transducer, patients were divided into two groups (Group 1 = 8 seconds, Group 2 = 10 s). The treatment parameters were as follows: frequency = 21 MHz, sectors activated = 6, acoustic power = 2.45w, time between shots = 20 s. All patients were treated under peribulbar anesthesia. The patient was laid supine, the coupling cone was centered on the patient's eye, and the treatment probe was inserted into the cone. The cone was held in place by low vacuum suction, and the transducers were sequentially activated automatically by continuous pressing of the foot switch. The overall procedure duration was <5 min. Posttreatment regime included topical loteprednol (L-Pred, Allergan, Irvine, CA), homatropine (Homide, Indoco Remedies, Goa, India) and Nepafenac (Nevanac, Alcon Laboratories, Fort Worth, TX). Preoperative hypotensive medications were maintained unchanged in the postoperative period unless a favorable IOP response necessitated their withdrawal.

Patients were followed up at day-1, day-7, and month-1, 2, 3, 6, and 12. Best-corrected visual acuity, slit lamp biomicroscopy with dilated fundoscopy, and Goldmann applanation tonometry were performed at each visit. All IOP measurements were taken at the same time of the day as the preoperative IOPs. Mean IOP was calculated by taking the average of three measurements.

Endpoint measures and statistical analysis

The primary endpoint was IOP reduction at 6 and 12 months (response rate). Treatment response was defined as IOP reduction from baseline >20% and final IOP >5 mmHg without supplemental hypotensive medications and without re-intervention (complete success), whereas qualified success was defined as achieving the same with supplemental hypotensive medications. Failure was considered where (i) IOP was not reduced by 20%, (ii) IOP value was ≤5 mmHg on two consecutive follow-up visits, and (iii) additional intervention was necessary. In the case of additional treatment such as filtering surgery or cyclodestruction procedure (laser or cryotherapy), the patient was deemed as having failed the ultrasound treatment.

Secondary endpoints were a percentage of IOP reduction and success rates at each follow-up visit compared with baseline, number of hypotensive medications used and safety criteria. As per World Glaucoma Association guidelines, safety criteria were defined by the incidence of device/procedure-related side effects and percentage of eyes that lost 2 lines or more Snellen BCVA.[11]

Descriptive statistics (mean ± standard Deviation [SD]) was used to report demographic and ocular baseline characteristics. Frequency distribution and percentage were used for categorical data and mean ± SD for continuous variables. Wilcoxon rank sum test or Fisher's exact test was used for demographic analysis. For continuous variables, the nonparametric Mann–Whitney test was performed to detect the difference among groups. Statistical significance was set at $P < 0.05$, and SPSS software Version 17.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis.

Results

Patient characteristics

Patient characteristics, demographic, and ocular, are described in Table 1. Seventy-three eyes of 73 patients (54 males, 19 females, and mean age 62.4 years) were enrolled in the study. Group 1 (8 s) consisted of 28 patients, and Group 2 (10 s) consisted of 45 patients. A flow chart of patients is displayed in Fig. 2. In Group 1, 25 patients (89%) completed M6 and 19 patients (68%) completed M12 follow-up. In Group 2, corresponding figures were 43 patients (96%) for M6 and 40 patients (89%) for M12.

Efficacy

The graph showing mean IOP in all patients at each follow-up visit is shown in Fig. 3. In the entire population, IOP was significantly reduced from 23.5 mmHg (SD = 3.0 mmHg) to 15.8 mmHg (SD = 3.5 mmHg) corresponding to a mean reduction of 7.7 mmHg (32.3%) at 6 months ($P < 0.001$) and to 15.7 mmHg (SD = 5.4 mmHg) corresponding to a mean reduction of 7.8 mmHg (32.6%) at 12 months ($P < 0.001$). For all patients, successful IOP control as defined by >20% IOP decrease and IOP >5 mmHg was obtained in 77.9% (53/68) patients at 6 months. At 12 months, the same was obtained in 78.3% (47/60) patients. The IOP reduction for all patients is shown in Table 2.

When analyzing the results group-wise, the effect of ultrasound cycloplasty (UCP) treatment was clinically significant in both groups. The mean ± SD IOP at baseline and each follow-up visit with a mean number of glaucoma

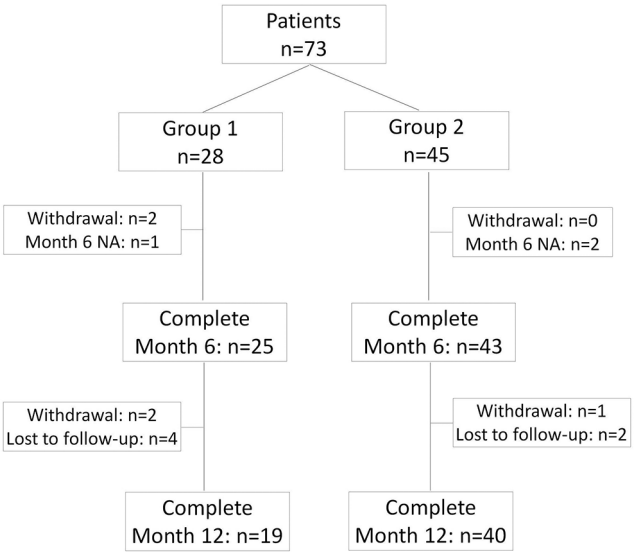

Figure 2: Flow chart of the study

Table 1: Demographic characteristics

	All population	Group 1	Group 2	*P*
Patients	73	28	45	
Age, mean±SD (range), year	62.4±12.9 (25-85)	64.8±11.6 (33-83)	61.0±13.6 (25-85)	0.3912[a]
Sex				0.7972[b]
Female	19	8	11	
Male	54	20	34	
Type of glaucoma				0.7022[b]
Primary open-angle	65	26	39	
Pigmentary	1	-	1	
Exfoliative	7	2	5	
Number of previous trabeculectomy				0.2911[b]
n=0	69	28	41	
n=1	4	0	4	
n≥2	0	0	0	
Preoperative mean values±SD				
IOP, mmHg	23.5±3.0	23.3±2.4	23.7±3.4	0.7160[a]
Number of glaucoma medications	0.7±0.9	0.5±0.6	0.7±1.0	0.5380[a]
BCVA, LogMar	0.319	0.287	0.345	0.9427[a]

[a]Mann-Whitney, [b]Fisher test. IOP: Intraocular pressure, BCVA: Best corrected visual acuity, SD: Standard deviation

Table 2: Intraocular pressure at baseline and during follow-up in all patients

	All patients			
	Mean±SD IOP mmHg (number of patients); mean glaucoma medications	Relative IOP reduction mmHg (%)	Response rate (%)	*P**
Baseline	23.5±3.0 (73); 0.7	NA	NA	
Day 1	14.2±5.1 (73); 0.7	39.6	82	<0.001
Day 7	12.4±4.4 (73); 0.7	47.1	93	<0.001
Month 1	14.5±5.0 (73); 0.6	37.6	85	<0.001
Month 2	15.6±4.0 (71); 0.7	33.1	76	<0.001
Month 3	15.5±3.8 (72); 0.8	33.7	81	<0.001
Month 6	15.8±3.5 (68); 0.9	32.3	78	<0.001
Month 12	15.7±5.4 (59); 1.0	32.6	78	<0.001

*Wilcoxon test. NA: Not available, IOP: Intraocular pressure, SD: Standard deviation

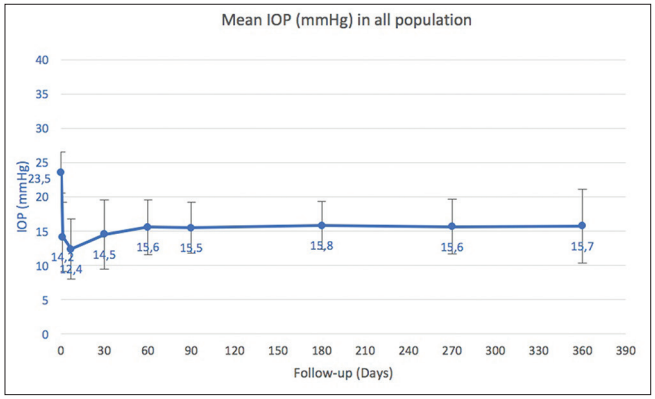

Figure 3: Graph showing intraocular pressure reduction (mean ± standard deviation in mm Hg) in all patients at baseline and each follow-up visit

medications used and corresponding IOP reduction in each group is shown in Table 3.

In Group 1, IOP was significantly reduced from 23.3 mmHg (SD = 2.4 mmHg) to 15.4 mmHg (SD = 3.5 mmHg) corresponding to a mean reduction of 7.9 mmHg (34%) at 6 months ($P < 0.001$), and the effect was sustained at 12 months (mean IOP = 14.3 mmHg [SD = 3.8 mmHg] corresponding to mean reduction of 9 mmHg [37.4%]) ($P < 0.001$). Successful IOP control was achieved in 80% of patients (20/25) at 6 months (mean IOP reduction of 37%), and in 79% of patients (15/19) at 12 months (mean IOP reduction of 45%). Rate of complete success was 56% (14/25) and 42% (8/19) at 6 months and 12 months, respectively. Corresponding figures for qualified success was 24% (6/25) and 37% (7/19). Failure rate was 20% (5/25) and 21% (4/19) at 6 and 12 months, respectively.

In group 2, IOP was significantly reduced from 23.7 mmHg (SD = 3.4 mmHg) to 16.1 mmHg (SD = 3.5 mmHg) corresponding to mean reduction of 7.6 mmHg (31.3%) at 6 months ($P < 0.001$), and the same was maintained at 12 months (mean IOP 16.4 mmHg [SD = 5.9 mmHg] corresponding to mean reduction of 7.3 mm Hg [30.4%]) ($P < 0.001$). Successful

Table 3: Intraocular pressure at baseline and during follow-up in Group 1 and 2

	Mean±SD IOP mmHg (no patients); mean glaucoma medications	Relative IOP reduction mmHg (%)	Success rate (%)	*P**
		Group 1 (8s)		
Baseline	23.3±2.4 (28); 0.5	NA	NA	
Day 1	15.3±5.4 (28); 0.5	34.6	75	<0.001
Day 7	13.2±4.3 (28); 0.5	43.4	89	<0.001
Month 1	15.9±5.0 (28); 0.5	31.3	75	<0.001
Month 2	16.8±4.3 (27); 0.7	26.6	67	<0.001
Month 3	16.1±3.5 (27); 0.9	30.5	70	<0.001
Month 6	15.4±3.5 (25); 1.0	34.0	80	<0.001
Month 12	14.3±3.8 (19); 1.2	37.4	79	<0.001
		Group 2 (10s)		
Baseline	23.7±3.4 (45); 0.8	NA	NA	
Day 1	13.4±4.7 (45); 0.8	42.7	87	<0.001
Day 7	11.9±4.4 (45); 0.8	49.4	96	<0.001
Month 1	13.7±5.0 (45); 0.7	41.5	91	<0.001
Month 2	14.8±3.6 (44); 0.7	37.1	82	<0.001
Month 3	15.1±3.9 (45); 0.7	35.6	87	<0.001
Month 6	16.1±3.5 (43); 0.8	31.3	77	<0.001
Month 12	16.4±5.9 (40); 1.0	30.4	78	<0.001

*Wilcoxon test. NA: Not available, SD: Standard deviation, IOP: Intraocular pressure

IOP control was achieved in 77% of patients (33/43) at 6 months (mean IOP reduction of 36%), and in 78% of patients (32/41) at 12 months (mean IOP reduction of 41%). The rate of complete success was 65% (28/43) and 51% (21/41) at 6 months and 12 months respectively. Corresponding figures for qualified success was 12% (5/43) and 27% (11/41). The failure rate was 23% (10/43) and 22% (9/41) at 6 and 12 months, respectively. The difference in IOP control between two groups at 12 months was not statistically significant (Fisher test, $P = 0.591$).

Safety profile

All patients underwent the procedure under peribulbar anesthesia. No complication occurred during any of the procedures. None of the patients reported pain during the procedure. Four patients (7%) had an intraoperative subconjunctival hemorrhage.

Early postoperative complications included conjunctival hyperemia in 68 patients (93%), minimal anterior chamber reaction in 67 patients (92%), superficial punctate keratitis in 4 patients (6.8%), and corneal epithelial defects in 3 patients (5.4%) which resolved with postoperative medications. No case of IOP spike following the procedure (IOP >baseline IOP + 10 mmHg in the first 7 days) occurred.

Late postoperative complications included scleral marks in 22 patients (30%), minimal peaking of the pupil in 10 patients (13.7%) and induced astigmatism (>1.0 Diopter) in 2 patients (2.7%). Peaking of the pupil was noted at the quadrant where the scleral mark was relatively closer to the limbus. Focal shrinkage of scleral tissue probably resulted in sectoral pupillary distortion and induced astigmatism. Three patients (4%) had postoperative hypotony (IOP <6 mmHg) of which one had a flat anterior chamber, unrecordable IOP and choroidal detachment which was treated with systemic steroids and choroidal drainage. The other two patients responded well to conservative management. One patient developed branch retinal vein occlusion with macular edema and was treated with an anti-VEGF injection and argon laser photocoagulation. None of the patients developed corneal burn or phthisis bulbi. The complications noted during and after the procedure are listed in Table 4.

Visual acuity

Mean BCVA was 0.319 logMar at the baseline visit and remained statistically unchanged at 0.316 logMar at the end of 12-month follow-up ($P = 0.943$). Transient change in the astigmatic correction of >1 Diopter was noted in two patients. Visual acuity loss of two lines or more was observed in six patients. This was due to the progression of preexisting cataract in two patients, and persistent superficial punctuate keratitis in two patients. One patient had persistent uveitis and worsening of end-stage glaucoma was noted in one patient. Scattergrams of preoperative versus postoperative visual acuity data in all patients at 12 months are displayed in Fig. 4.

Discussion

The present study was conducted to evaluate the efficacy and safety of UCP for the first time in Indian OAG patients. IOP reduced from a preoperative value of 23.5 ± 3.0 mmHg to 15.7 ± 5.4 mmHg (32.6% decrease) at 12 months. Successful IOP control as defined by >20% IOP decrease and IOP value >5 mmHg was obtained in 78.3% (47/60) patients at 12 months. The treatment was well tolerated with no incidence of long-term severe hypotony and phthisis bulbi, the most dreaded complications of cyclodestructive procedures.

Cyclodestruction has been the first choice for treatment of high-pressure glaucoma refractory to other modalities of treatment.[5,12] The trans-scleral diode CPC has practically

Table 4: Intra and postoperative complications

Ocular complications	All population	Group 1	Group 2	*P**
Intraoperative (%)				
Subconjunctival hemorrhage	4 (7)	2 (7)	2 (4)	0.6349
Postoperative (%)				
Hyperemia	68 (93)	26 (93)	43 (93)	0.6349
Anterior chamber reaction (<7 days)	67 (92)	25 (89)	42 (92)	0.6691
Ocular pain (<1 day)	36 (49)	21 (75)	15 (33)	0.0007
Scleral marks	22 (30)	6 (21)	16 (35)	0.2945
Minor pupil peak	10 (14)	5 (18)	5 (11)	0.4923
Superficial punctate keratitis	4 (7)	4 (14)	-	NA
Transient hypotony	3 (5)	1 (4)	2 (4)	1
Corneal epithelial defect/edema	3 (5)	2 (7)	1 (2)	0.5543
Astigmatism (>1 diopter)	2 (4)	-	2 (4)	NA
Transient hypotony with choroidal detachment	1 (1)	1 (4)	-	NA
Transient macular edema	1 (1)	1 (4)	-	NA
Mild mydriasis	1 (1)	-	1 (2)	NA
Phthisis	-	-	-	NA
Induced cataract	-	-	-	NA

*Fisher test. NA: Not available

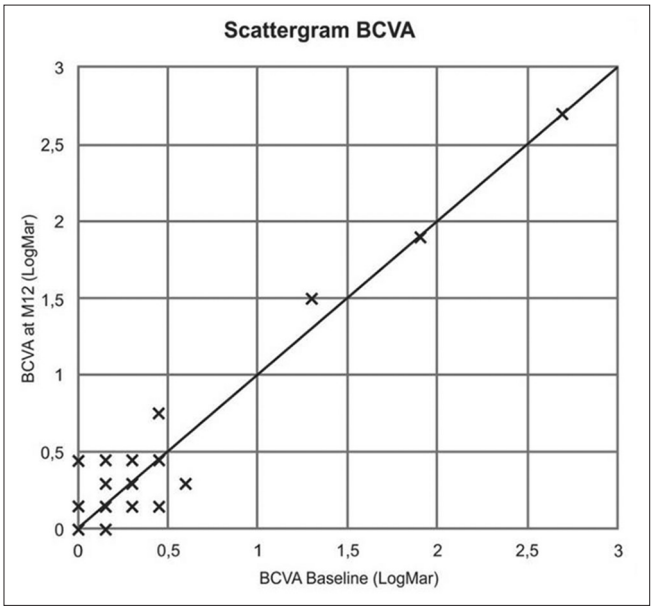

Figure 4: Scattergram showing the preoperative visual acuity (x-axis) versus postoperative 12 months visual acuity (y-axis) in all patients

replaced the cyclocryo and the neodymium-doped yttrium aluminum garnet laser ablation, due to comparable efficacy and increased safety and tolerability.[13,14] However, the therapeutic effect of diode CPC can be lost over time, which necessitates retreatment in a considerable number of cases. The occurrence of sight-threatening complications such as persistent hypotony and phthisis caused by excessive collateral tissue damage limits its use in eyes with useful vision.[15,16]

UCP is an exciting innovation which consists of the application of HIFU to selectively treat the ciliary processes in a single-step, computer-assisted and highly reproducible manner, first described by Aptel *et al*.[8] The focal cyclodestruction preserves adjacent structures and causes controlled reduction in aqueous humor production, thereby minimizing intraoperative and postoperative complications. The minimal ocular surface involvement ensures faster patient recovery and facilitates retreatment if necessary. The procedure is rapid (<3 min), noninvasive and can be performed in daycare set-up. In multiple studies conducted across Europe, UCP has been shown to be an effective and safe method to control IOP in patients with refractory and nonrefractory glaucoma.[17-21]

In our study, the efficacy of IOP control with UCP (33% mean reduction at 12 months) corresponded well to that noted in previous studies (mean IOP reduction at 12 months ranging between 30% and 38%).[19-21] In this study, only 4 out of 73 patients with OAG had a history of prior glaucoma surgery, whereas the earlier studies comprised a mixed population of primary and secondary glaucoma with at least one filtration surgery.[18-20] Therefore, the type of glaucoma and history of trabeculectomy did not have much bearing on the efficacy. In this respect, the study is more comparable to that by Aptel *et al*. who noted 30% IOP control in patients naïve of previous filtration surgery.[21]

With regard to the ultrasound time, Denis *et al*. found better IOP control with 6s versus 4s treatment with the first generation probe.[20] Giannaccare *et al*. noted improved efficacy with the second generation probe (8s treatment) compared to the first generation (4 and 6s treatment per transducer).[17] The 8s protocol with the second generation probe is commonly used in Europe. We chose the 8 and 10s protocol to assess whether prolonged treatment time has any bearing on efficacy or safety. We did not notice any significant difference in IOP reduction across the two exposure times (45% in Group 1 vs. 41% in Group 2). However, patients in Group 2 had a higher incidence of anterior chamber reaction and scleral marks compared to Group 1 patients.

Scleral marks, i.e. grayish circumlinear spots concentric to the limbus noted at the ultrasound entry point in one or

multiple sectors were seen in 30% of the study population, more in Group 2 (35%) than in Group 1 (21%). These are well-delineated foci of scleral thinning without any sign of inflammation or ectasia. Mastropasqua *et al*.[22] using anterior OCT have revealed intrascleral hyporeflective spaces with altered internal reflectivity within the stroma at the site of transducer contact. They hypothesized their occurrence to heat-induced scleral fiber delamination. These probably resulted in a change of refractive status (esp. astigmatic correction) and pupillary abnormalities (mydriasis, sectoral peaking) in a small number of patients. These effects resolved over time and were not visually or esthetically significant. Due to the limited circumference (45%) of sclera treated with the six transducers and well delineated nature of the scleral marks, post-UCP scleral remodeling is unlikely to interfere with future repeat therapy or a future trabeculectomy. Three patients who has postoperative hypotony had additional comorbidities and responded well to treatment with good visual recovery. In contrary to studies reporting 17%–39% risk of vision loss and hypotony with diode CPC,[6,7,13,15,16] no sight threatening complications such as scleral ectasia, corneal burn, and phthisis were reported in the present study.

We used the second generation probe in our study, which in comparison with the earlier probe, allowed improved positioning and avoidance of air bubbles acting as cold spots interfering with the passage of ultrasound energy. The increased transducer size enabled a larger treatment zone, thereby nullifying the effect of anatomical variations in the ciliary body. All these contributed to the efficacy and reproducibility of the outcome. However, the small sample size, uneven distribution of patients in groups and a limited follow-up period constitute the limitations of the study. Further prospective randomized clinical trials are required to compare the efficacy and safety of UCP vis-à-vis diode CPC and filtration surgery.

Conclusion

UCP is an effective and well-tolerated method of IOP control in OAG. Our short-term results in Indian eyes are comparable to that in the Caucasian population. Further research is ongoing to study the IOP control at longer follow-up period as well as to extend its indication to angle closure and secondary glaucoma.

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Conflicts of interest

There are no conflicts of interest.

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