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Efficacy and safety of ultrasound cycloplasty in Indian eyes with open-angle glaucoma

Chandrima Paul, Divya J[1], Subhrangshu Sengupta[2], Richa Kamal[3], Anujeet Paul[4], Ishani Mitra[5]

Purpose: To evaluate the safety and efficacy of ultrasound cycloplasty in eyes with primary or secondary open-angle glaucoma, not amenable to adequate control of intra-ocular pressure (IOP) with medical treatment. **Methods:** Prospective interventional cohort study of 28 eyes of 28 subjects in a tertiary eye care centre in India in patients with open-angle glaucoma. All enrolled eyes underwent ultrasound cycloplasty with the second-generation probe with six shots of 8 s each, operated by a single surgeon between November 2018 and January 2020. They were followed up for a period of 12 months. The primary treatment outcome was IOP and the secondary outcomes were vision and postoperative complications. **Results:** A total of 28 eyes of 28 patients were studied, and the mean age was 63.82 ± 6.46 years. Primary open-angle glaucoma (75%) was the most common etiology. There was significant reduction in IOP from the baseline (24.93 ± 4.27 mmHg) to the postoperative value (15.82 ± 3.14 mmHg) at the end of 12 months ($P < 0.00001$). Mean reduction in IOP was 9.14 ± 4.09 mmHg at 12 months (36.66%). Number of ocular hypotensives reduced significantly from baseline (3.32 ± 0.47) to 12-month postoperative follow-up (0.68 ± 0.74) ($P < 0.00001$). Qualified success was achieved in 89.28% eyes. No major complications were noted. **Conclusion:** Ultrasound cycloplasty is found to be effective and safe in eyes with open-angle glaucoma because of the primary or secondary etiology, being more effective in the former.

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Glaucoma is a public health problem affecting 100 million people worldwide.[1] Control of intra-ocular pressure (IOP) is the only available modality of treatment to halt the progression of the disease process.[2] This can be achieved through medical means, including medications and lasers, surgical means, or a combination of the two.[2-4] Coagulation necrosis of the ciliary body may be induced as a method of reducing IOP by decreasing the secretion of aqueous humor. It is of much value in refractory glaucoma, not amenable to other modalities of treatment. However, because of the lack of selective tissue targeting, unpredictable dose-response relationship, and the possibility of vision-threatening complications, these procedures are often limited to end-stage glaucoma resistant to conventional medical and surgical treatment modalities.[3,5-13]

Endoscopic cyclophotocoagulation is safer than trans-scleral cyclophotocoagulation, but is an invasive procedure.[14-17] It still has adverse effects, including increased inflammation, IOP spikes, and dislocation of the intra-ocular lens.[18,19]

High-intensity focused ultrasound (HIFU) technology is a method of ciliary body ablation that had been advocated in the 1980s.[20] Ultrasound cycloplasty (UCP) that employs HIFU provides more selective coagulation of the ciliary body and minimizes the damage to the adjacent structures by focusing at the desired depth and area.[13,21-28] It also increases suprachoroidal and trans-scleral uveoscleral outflow.[29]

In this study, we aim to study the safety and efficacy of UCP in Indian eyes with primary or secondary open-angle glaucoma.

Methods

This was a prospective interventional cohort study conducted in a tertiary eye care centre in India of 28 eyes of 28 patients with primary or secondary open-angle glaucoma, not achieving target IOP with three different ocular hypotensive medications. It was a single-centre, single-surgeon study; participants recruited between November 2018 and January 2020. Approval was obtained from the institutional ethics committee and was conducted in accordance with the tenets of the declaration of Helsinki.

Eyes with diagnosed primary or secondary open-angle glaucoma ≥18 years of age were included. Eyes previously operated for IOP control were excluded. Eyes with causes of visual loss unrelated to the glaucoma were excluded.

Preoperatively vision, IOP (Goldmann applanation tonometry), slit lamp biomicroscopy, and gonioscopy were recorded. Glaucoma was diagnosed in accordance with the

Director, [1]Fellow, Comprehensive Ophthalmology, [3]Vitreo-Retina Services, B B Eye Foundation, Kolkata, West Bengal, [2]Centre for Sight, Kolkata, West Bengal, [4]Mahatma Gandhi Medical College and Research Institute, Pondicherry, [5]Fortis Hospital, Bangalore, Karnataka, India

Correspondence to: Dr. Chandrima Paul, 2/5, Sarat Bose Road, Sukhsagar, Near Minto Park, Bhowanipore, Kolkata - 700 020, West Bengal, India. E-mail: drchandrimapaul@gmail.com

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International Society of Geographical and Epidemiologic Ophthalmology classification.[30]

The eyes were treated by UCP, performed using the second-generation probe (EyeOP1, Eye Tech care; France) under peribulbar anesthesia using 2% lignocaine. The procedure was performed in six sectors at an operating frequency of 21 MHz with acoustic power of 2.45 W and shot duration of 8 s with interval of 20 s. The coupling cone was centered on the eye and kept in place with low vacuum suction and filled with balanced salt solution, followed by introduction of the treatment probe inside the cone. The transducer was then activated by pressing the foot switch.

Primary outcome was the postoperative IOP. Reduction of IOP by ≥15% from the baseline and <21 mmHg and ≥5 mmHg with or without one ocular hypotensive was defined as success. The patients were followed up for a period of 12 months. Follow-up visits were conducted on the first day and after 1 week, 2 weeks, 6 weeks, 3 months, 6 months, and 12 months postoperatively. At each visit, vision and IOP were recorded. Slit lamp biomicroscopic examination was done. Visual fields and optic disc photography were performed 6 and 12 months postoperatively.

Postoperatively, moxifloxacin 0.05% eye drops six times daily for 2 weeks and prednisolone acetate 1% eye drops six times daily for 1 week, gradually tapered and stopped over 4 weeks were prescribed for all eyes. Anti-glaucoma medications were titrated to the IOP.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 25. Quantitative data were described as means (±SD) and qualitative data were described as numbers and percentages. Comparisons between preoperative and postoperative parameters were done using Wilcoxon signed rank test and Freidman test. *P* value ≤0.05 was considered to be statistically significant. Wilcoxon signed rank test has been used here as opposed to repeated measures ANOVA as related samples are being compared. Also, their performance is comparable.

Results

Demographics

A total of 28 eyes of 28 patients with glaucoma not achieving target IOP with at least three different ocular hypotensives underwent UCP and were followed up for 1 year. The mean age was 63.82 ± 6.46 years with 46.43% males and 53.57% females. The most common etiology for rise in IOP was primary open-angle glaucoma (POAG) (75%). Details of the demography and baseline clinical data of the sample are given in Table 1.

Table 1: Demographic and baseline clinical data of the sample

Male:Female	1: 1.15	*n*=13 (male), 15 (female)
Number of phakic eyes	17	
Number of pseudophakic eyes	11	
Etiology	POAG (75%)	*n*=21
	PEX (14.28%)	*n*=4
	PDG (3.57%)	*n*=1
	NVG (7.14%)	*n*=2
	Mean±SD	Range
Age	63.82±6.46 years	51-74 years
IOP	24.93±4.27 mmHg	22-34 mmHg
BDVA	0.40±0.20 logMAR	
Number of ocular hypotensives	3.32±0.47	3-4

POAG=primary open-angle glaucoma, PEX=pseudoexfoliation, PDG=pigment dispersion glaucoma, NVG=neovascular glaucoma, BDVA=best distance visual acuity, IOP=intra-ocular pressure

Table 2: Postoperative IOP and IOP reduction at successive follow-up visits

	Mean IOP (mmHg)	*P*	% Reduction in IOP
Day 1	12.71±2.68	<0.00001	48.98
1 week	13.00±2.94	<0.00001	48.41
2 weeks	13.36±2.65	<0.00001	47.69
6 weeks	13.96±2.77	<0.00001	45.29
3 months	14.36±2.78	<0.00001	43.68
6 months	14.96±3.09	<0.00001	41.27
12 months	15.82±3.14	<0.00001	36.66

IOP=intra-ocular pressure

Efficacy

Mean IOP was found to be significantly less in each postoperative visit compared to the baseline IOP ($P < 0.00001$). Table 2 and Fig. 1 show the fall of IOP at each postoperative visit and at 12 months, respectively, in comparison with the baseline IOP. There was a mean reduction in IOP of 9.14 ± 4.09 mmHg at the end of 12 months from baseline. Maximumreduction in IOP from baseline was obtained on day 1. This was followed by a small rise in IOP over the subsequent follow-up visits as depicted in Fig. 1.

Mean number of ocular hypotensives reduced significantly in the postoperative period from a baseline value of 3.32 ± 0.47 to 0.68 ± 0.74 ($P < 0.00001$) 12 months after UCP.

Qualified success was achieved in 89.28% eyes ($n = 25$) at the last follow-up visit. Of the three eyes that failed to achieve the target IOP, two eyes had secondary glaucoma and one had POAG. Of the eyes with secondary glaucoma, one eye had pseudoexfoliation (PEX) and the other had neovascular glaucoma (NVG). About 95.23% of eyes with POAG, 75% of eyes with PEX, 50% of eyes with NVG, and 100% of eyes with pigment dispersion glaucoma (PDG) achieved qualified success. The eyes with POAG and PEX underwent filtering procedure after the study period and the eye with NVG was treated successfully by diode laser cyclophotocoagulation.

About 12 months after UCP, there was no significant change in best distance visual acuity (BDVA) ($P = 0.33$). The mean BDVA showed an initial worsening attributable to anterior chamber reaction. This was followed by resolution of inflammation and return to near baseline levels at 2 weeks post procedure. This is depicted in Fig. 2.

None of the eyes had significant intra-operative or postoperative complications. There was no recorded IOP spike. However, severe conjunctival injection with anterior

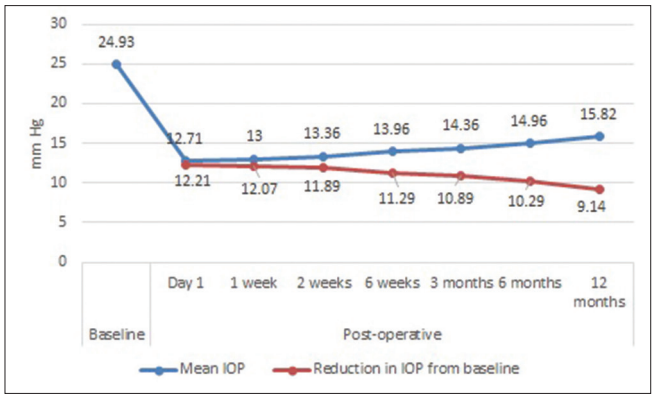

Figure 1: Changes in mean intra-ocular pressure (IOP) from baseline and reduction of IOP until 12 months postoperatively

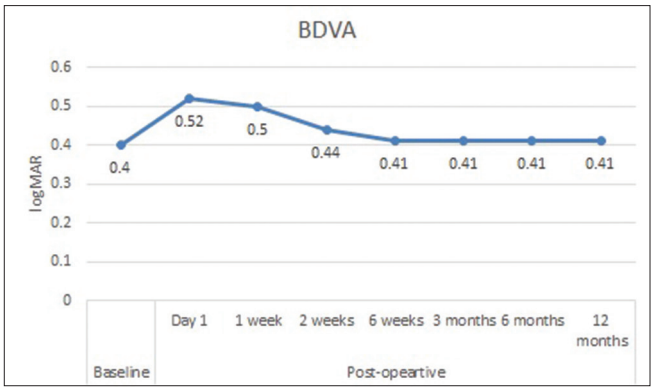

Figure 2: Mean best distance visual acuity before the procedure and at each postoperative visit

chamber cells and flare was noted in nine of the 28 eyes. This was successfully managed by topical steroid eye drops in the postoperative regimen.

Discussion

UCP has revolutionised cyclo-destruction by precise targeting of tissue by higher frequency and direct contact, thus, yielding better results through its dual action.[31] Multiple studies have evaluated the efficacy and safety of UCP in the past. This study was aimed at studying the safety and efficacy of UCP in Indian eyes. A total of 28 eyes with inadequate IOP control with maximum medication were treated by UCP and followed up for a period of 12 months.

The mean IOP in the postoperative period was significantly lesser at each follow-up compared to the baseline value. At 12 months postoperatively, the mean reduction in IOP from baseline was 36.66 ± 16.40%. This is well within the range of IOP reduction in previous studies that ranged from 30% to 42.3%.[22,32-34] Higher and lower degrees of reduction in IOP may be attributable to the composition of the sample. While we achieved higher success rates in POAG and PDG followed by PEX and then NVG, the sample size of secondary glaucoma was too little to comment on the same. Giannaccare *et al*.[28] have also obtained greater reduction in IOP in eyes with POAG. They also observed that eyes with higher baseline IOP had poorer response to UCP in comparison with eyes with lower baseline IOP. Deb-Joardar*et al*.[35] obtained a 41% IOP reduction that is also within the mentioned range of IOP reduction obtained.

We obtained qualified success in 89.28% of the eyes. This is higher in comparison with a previous study by Torky *et al*. (77.4%).[34] However, this might be attributable to our criteria for success mandating only ≥15% reduction from baseline IOP, whereas the study being compared with required ≥30% IOP reduction from baseline. An overall success of 78.3% was obtained in the study by Deb-Joardar *et al*.[35]

A slight increase in mean IOP was noted in the 12 month follow-up compared to the day 1 follow-up. It is to be noted that this is expected because of the re-epithelialization of the ciliary processes over the months, with partial functional recovery as well.[36-38]

No significant deterioration in vision was noted 12 months postoperatively and none of the eyes had any major complications. This is in accordance with other studies where UCP has been tolerated well.[22,33,34,39,40] This advantage sets it apart from other cyclodestructive procedures and, thus, UCP may be considered even for eyes with good visual acuity and early glaucoma.

Despite the betterment in safety of the procedure, UCP is still known to cause alterations in the scleral morphology.[41] Indian eyes have a reported higher incidence of sclera marks compared with Caucasian eyes, probably owing to the pigmentation.[42] However, we did not encounter any scleral pigmentation or scarring in any of the eyes studied.

This study is limited by some factors that include a small sample size, shorter follow-up than desirable, exclusion of angle-closure glaucoma, and previously operated eyes, a heterogenous distribution across the various forms of glaucoma making the comparison between them difficult and lack of comparison with a standardised surgical approach for the type of glaucoma. Randomized controlled trial with larger sample size and longer follow-up comparing various exposure times are necessary to further establish the safety and efficacy of this procedure and make it possible to apply this treatment modality to a wider range of conditions.

Conclusion

We may conclude that UCP is an effective and safe modality of treatment for eyes with open-angle glaucoma because of the primary or secondary etiology.

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Conflicts of interest

There are no conflicts of interest.

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