• Clinical Research •

Efficacy of ultrasound cyclo-plasty in patients with refractory glaucoma

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Abstract

● **AIM:** To assess the efficacy and safety of ultrasound cyclo-plasty (UCP) in lowering intraocular pressure (IOP) among Chinese patients suffering from refractory glaucoma.

● **METHODS:** In this 12-month retrospective study, 28 patients with refractory glaucoma (IOP≥25 mm Hg) were treated with 8-second UCP using either 8 or 10 probe sectors. The principal measure of efficacy was the decrease in IOP at the following intervals after UCP: 1d, 1, 3, 6, and 12mo, with each measurement compared to baseline.

● **RESULTS:** Mean IOP (in mm Hg) was reduced from 46.8±8.9 to 24.5±3.2, 27.0±4.8, 29.1±4.6, 26.1±4.5, and 28.3±4.8 at 1d, 1, 3, 6, and 12mo postoperatively, respectively. Compared to baseline, IOP reductions at these time points were 45.0%, 39.9%, 35.3%, 41.4%, and 36.7%, respectively. Most patients experienced relief from ocular pain after surgery. No cases of choroidal detachment or hypotony was observed.

● **CONCLUSION:** UCP is effective in reducing IOP among Chinese patients with refractory glaucoma and shows a favorable safety profile.

● **KEYWORDS:** ultrasound cyclo-plasty; refractory glaucoma; intraocular pressure

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INTRODUCTION

Glaucoma, ranking as the second most common cause of blindness globally, is a type of neurodegenerative condition marked by the ongoing degeneration of the retinal ganglion cells[1]. Refractory glaucoma is a subtype of the condition where patients demonstrate resistance to conventional surgical treatments, resulting in either repeated treatment failures or a predicted low likelihood of success if attempted as an initial intervention[2-3]. Standard treatments for glaucoma typically include laser therapy and conventional surgeries such as trabeculectomy or tube shunt surgery.

Managing refractory glaucoma can be challenging, requiring alternative or more aggressive approaches, such as complex surgeries or newer surgical techniques. Each case is evaluated individually to determine the best course of action based on the type of glaucoma, previous treatments, and the patient's overall health[4-6].

Ultrasound cyclo-plasty (UCP) represents a significant innovation in the realm of cycloablation, offering a safe and effective alternative for the reduction of intraocular pressure (IOP) in glaucoma treatment. A notable progression within this domain is marked by the creation of a device that incorporates compact transducers, which are the cornerstone of UCP technology. This device stands out due to its precision and minimally invasive approach. The advent of UCP has not only enhanced the safety profile of cycloablation procedures but also expanded the treatment options available to clinicians and their patients[7-9].

The primary mechanism underlying the UCP procedure is the change of the ciliary body epithelium, which reduces the production of aqueous humor. Supporting evidence from both animal and human studies has highlighted the role of increased uveoscleral outflow in UCP's mechanism[7,10-11].

Previous studies about UCP primarily used a procedure with 6 transducers, varying treatment duration to assess the effect of different dosages on efficacy and safety. Some studies have also examined the benefits and risks of multiple UCP

sessions[12-13], including second or third procedures for patients with suboptimal responses to the initial treatment. Standard UCP involves a single procedure targeting six sectors of the ciliary body, with the dose determined by the therapeutic area extent. High-dose UCP increases the treated circumference by targeting more sectors[14-17]. This study will test the efficacy and safety of UCP procedures activating 8 or 10 sectors for managing refractory glaucoma in Chinese patients.

PARTICIPANTS AND METHODS

Ethical Approval This single-arm, retrospective, institutional investigation was conducted and documented following the World Glaucoma Association's guidelines for ophthalmic surgical studies and adhering to the ethical principles of the Declaration of Helsinki. The research plan received clearance from the Ruijin Hospital's Ethics Committee (2021-RJCER-90). Participants offered their written agreement to take part in the research. The study took place from May 2022 to July 2023, with retrospective data analysis.

Inclusion Criteria 1) Age 18 to 80y; 2) Patients who had failed one or more previous filtration surgeries or a predicted low likelihood of success if attempted as a conventional anti-glaucoma surgery and whose maximum medicated IOP was ≥25 mm Hg; 3) Ability and willingness to attend all scheduled appointments.

Exclusion Criteria 1) Recent surgical or laser treatment (within 3mo); 2) Cognitive impairment affecting consent or study compliance; 3) Concurrent systemic medications affecting IOP; 4) Ocular tumor or retinal detachment; 5) Ocular infection; 6) Severe systemic illness.

Preoperative ophthalmic examinations included axial length measurements and white-to-white using an optical biometer (Lenstar LS 900, Haag-Streit, Switzerland) and ultrasound biomicroscopy (UBM, Quantel Medical Instruments). Data on best-corrected visual acuity (BCVA), Goldman applanation tonometry and slit-lamp biomicroscopy were collected.

Procedure The UCP device (EyeOP1, Eye Tech Care, France) equipped with 6 piezoelectric transducers was utilized, which is using high-intensity focused ultrasound. Patients were treated under topical and retrobulbar anesthesia (lidocaine and ropivacaine mixture). The standard UCP procedure involved: Applying a low-level vacuum attached with a suction ring at its base of the coupling cone to maintain eye contact; Inserting a ring with 6 active piezoelectric transducers into the cone; Filling the space with sterile water for injection to propagate sound waves; Performing a negative pressure test; Treating 8 or 10 probe sectors based on preoperative IOP (8 sectors for IOP<40 mm Hg, 10 sectors for IOP≥40 mm Hg), with each transducer activated for 8s and a 20-second interval between shots. The same surgeon performed all UCP procedures. The determination of the ultrasound probe size (12 or 13 mm) was based on the measurements of white-to-white and axial length before surgery.

Postoperative treatment included continuing preoperative pressure-lowering medications for 1mo and using dexamethasone (Tobradex, Alcon Laboratories, Inc., USA) four times every day for 1mo.

Statistical Analysis The statistical analysis was conducted utilizing the statistical software (SPSS, version 19.0). A paired sample *t*-test compared pre- and post-UCP treatment IOP. The threshold for statistical significance was established at $P<0.05$.

RESULTS

Patient Demography Demographic information of the patients is presented in Table 1. The study included 28 patients (16 males, 12 females) monitored for 12mo. Treatment was administered based on baseline IOP (8 or 10 sectors). Most patients had neovascular glaucoma (75%). Non-neovascuar glaucoma includes patients with glaucoma that still cannot control IOP after two filtration surgeries (4 cases), glaucoma caused by complex eye trauma (1 case) and glaucoma secondary to vitrectomy surgery (2 cases). All patients had light perception (LP) or no LP (NLP) vision, with the primary surgical goal being pain relief through IOP reduction.

Efficacy The effect of the UCP for patients with refractory glaucoma was clinically significant. The average and proportional decreases in IOP from the initial measurement to subsequent assessments are detailed in Table 2.

Table 1 Patient demographics *n* (%)

Demographics	*n*=28
Age (mean±SD), y	50.9±16.7
Male/female	16/12
Glaucoma type	
Neovascular glaucoma	21 (75.0)
Non-neovascuar glaucoma	7 (25.0)
Baseline vision acuity	
NLP	22 (78.6)
LP	6 (21.4)
Baseline IOP (mean±SD), mm Hg	46.8±8.9
Baseline IOP<40 mm Hg	7 (25.0)
Baseline IOP≥40 mm Hg	21 (75.0)
Number of glaucoma medications (mean±SD)	3.4

SD: Standard deviation; IOP: Intraocular pressure; NLP: No light perception; LP: Light peroption.

Table 2 Pre-surgical and post-surgical mean IOP

IOP	Mean IOP (mm Hg)	Relative IOP reduction (%)	Number of glaucoma medications
Baseline	46.8±8.9		3.4
Day 1	24.5±3.2[a]	45.0	3.4
Month 1	27.0±4.8[a]	39.9	3.1
Month 3	29.1±4.6[a]	35.3	1.9
Month 6	26.1±4.5[a]	41.4	2.5
Month 12	28.3±4.8[a]	36.7	2.6

IOP: Intraocular pressure. [a]$P<0.01$ *vs* baseline.

Table 3 Complications after surgery

Complications	Ocular pain	Subconjunctival hemorrhage	Anterior chamber reaction	Choroidal detachment	Hypotony
Day 1	6	21	4	0	0
Month 1	11	0	1	0	0
Month 3	8	0	0	0	0
Month 6	5	0	0	0	0
Month 12	6	0	0	0	0

At the 1st day after the UCP, the IOP significantly decreased from 46.8±8.9 to 24.5±3.2 mm Hg (P<0.01). At 1mo after UCP, the IOP was 27.0±4.8 mm Hg. The outcomes were derived with the glaucoma medication remaining unchanged.

At 3, 6, and 12mo, IOP was 29.1±4.6, 26.1±4.5, and 28.3±4.8 mm Hg. This translates to average reductions of 35.3%, 41.4%, and 36.7% respectively, these results were accompanied by a reduction in the quantity of glaucoma medications administered.

Complications Postoperative complications were listed in Table 3. Most patients experienced relief from ocular pain post-surgery. Minor complications included subconjunctival hemorrhage (21 patients) and anterior chamber reaction (4 patients), both resolving by the 1-month follow-up. No choroidal detachment or hypotony occurred.

DISCUSSION

In summary, the UCP procedure demonstrates significant potential as a groundbreaking treatment for glaucoma, providing a robust safety and efficacy profile. Our research, conducted over a 12-month follow-up period with Chinese patients suffering from refractory glaucoma, confirms the substantial reduction in IOP achieved by UCP. The mean IOP was reduced from a baseline of 46.8±8.9 mm Hg to 28.3±4.8 mm Hg at 12mo (P<0.01), representing an average reduction of 36.7%. This result aligns with previous research both domestically and internationally[13-15], which reported a decrease in IOP within 6 to 12mo post-UCP surgery ranging from 29.6% to 42.0%[15-17].

The UCP technique has evolved from traditional cyclodestructive methods by employing miniaturized transducers, such as those used in the EyeOP1 system by Eye Tech Care, France[18-20]. This advancement allows about 40% of the ciliary body was treated, with the capability to extend to 55% by rotating the probe. A short-term retrospective study comparing the IOP reduction between 8-sector and 10-sector UCP therapies revealed a more pronounced early reduction with the 8-sector approach. However, by the 3-month mark, no significant difference in IOP reduction or success rate was observed, suggesting that for patients with very high IOP, 10 sector UCP therapy might be more effective[21].

The UCP procedure has consistently been reported as safe, with minimal and transient complications such as choroidal detachment and intraocular inflammation. Severe complications like hypotony and phthisis, common in other cyclodestructive procedures, are rare with UCP[14-16,18,20].

In our study, no cases of choroidal detachment or hypotony were observed during therapeutic procedures. The limitations of this research include its relatively small sample size and non-comparative design. Future research should include larger cohorts and comparative groups to evaluate the response of various glaucoma subtypes to UCP. Additionally, with ongoing advancements, including the development of micropulse modes, there is a need for comparative studies to determine the optimal therapeutic strategy for glaucoma patients.

In this study, the majority of cases were of neovascular glaucoma, all of them had experienced failure of more than one drainage surgery (including conventional trabeculectomy, drainage valve implantation, *etc*.) and were unwilling to undergo surgery again or were not suitable for surgery due to systemic conditions. All patients had vision below the level of LP, and their main problem was ocular pain and discomfort. During the one-year follow-up after receiving non-invasive UCP surgery, most patients' pain was relieved. But in neovascular glaucoma there are ischemic areas requiring ablation to avoid the VEGF release, and the angle fibrovascular occlusion requiring a possible by-pass[22]. For patients with refractory glaucoma, simple UCP surgery may not be sufficient to achieve the target IOP, and repeated UCP or combination with other surgical methods may need to be considered.

In conclusion, UCP treatment is an effective and well-tolerated procedure for reducing IOP among patients with refractory glaucoma. It offers a valuable alternative to conventional treatments, although further research is necessary to refine treatment protocols and maximize patient outcomes. New technologies in the field of UCP, such as micropulse modalities, opens avenues for future studies that could provide even more effective and safer treatment options for glaucoma patients.

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