Eye (2021) 35:2499–2505
https://doi.org/10.1038/s41433-020-01260-9

The ROYAL COLLEGE of OPHTHALMOLOGISTS

ARTICLE

Effect of high-intensity focused ultrasound (HiFU) treatment on intraocular pressure and aqueous humour dynamics: 12 -months results

Anindyt Nagar[1,2] · Arij Daas[1,2] · Lina Danieliute[1,2] · Pouya Alaghband[1,2] · Cynthia Yu-Wai-Man[1,2] · Andrew Amon[1] · Elizabeth Galvis[1] · Kin Sheng Lim[1,2]

Received: 19 May 2020 / Revised: 10 September 2020 / Accepted: 22 October 2020 / Published online: 6 November 2020

Abstract

Purpose High intensity focused ultrasound (HiFU) is a cyclodestructive therapy for controlling intraocular pressure (IOP) in glaucoma. The mechanism of action is thought to be through destruction of the ciliary epithelium as well as increased uveoscleral outflow. We reviewed the change in aqueous humour dynamics parameters including aqueous humour flow rate, tonographic outflow facility (TOF) and uveoscleral outflow at 12 months.

Patients and methods This is a prospective observational study. Consecutive patients with open angle glaucoma (OAG) or ocular hypertension (OHT) requiring further IOP lowering were enroled in the study between August 2016 and January 2017. Patients were commenced on medication washout period prior to baseline and twelve months' visit.

Results Sixteen patients (OAG) in the treatment group underwent assessment at twelve months follow up. Mean age was 63.1 ± 11 years. Eleven patients were African/Caribbean and 5 were Caucasian. Nine patients were female and 7 were male. Mean post-washout IOP was reduced by 21% (28.3 ± 5.7 at baseline vs 22.4 ± 8.4 mmHg at 12 months, $p = 0.04$). Aqueous humour flow rate was reduced by 16% at twelve months (2.40 ± 0.6 at baseline vs 2.02 ± 0.6 µl/min at 12 months, $p = 0.0493$). There was no statistically significant change in the TOF (0.12 ± 0.09 at baseline vs 0.08 ± 0.05 µl/min/mmHg at 12 months, $p = 0.08$) or uveoscleral outflow (0.6 ± 1.3 at baseline vs 1.3 ± 0.85 µl/min at 12 months, $p = 0.15$).

Conclusion In this study, we demonstrated that the observed IOP reduction was likely due to aqueous humour flow rate reduction. The TOF and uveoscleral outflow were not detectibly changed.

Introduction

Glaucoma is the leading cause of irreversible blindness affecting 76 million patients worldwide and its prevalence is estimated to increase to 112 million by 2040 [1]. Raised intraocular pressure (IOP) remains the most important and only modifiable risk factor to alter the progression of disease or visual field loss [2, 3]. Lowering IOP can be achieved by two methods: (i) improving aqueous humour outflow by means of medications, laser or incisional surgery or (ii) reducing the production of aqueous humour by medications or cyclodestructive procedures. These techniques often cause collateral tissue damage, have an unpredictable dose-effect relationship and a high rate of complications [4–6] hence, cyclodestructive treatments have been used only in cases with refractory glaucoma or poor visual potential. The most popular method is to utilise 810 nm diode laser which can be delivered either transsclerally [7] (TSCP) or endoscopically (ECP).

More recently, high intensity focused ultrasound (HiFU) has provided an alternative technique [8, 9]. This is aimed at selective coagulation of the ciliary body without damaging adjacent tissues [10, 11]. EyeTech-Care (Rillieux-la-Pape, France) introduced a new ultrasound cycloplasty device called the EyeOP1 in 2011 [12] which delivers ultrasound energy to the ciliary body with pre-set parameters (it has received CE mark in May 2011 and Chinese FDA approval in October 2017). Studies have reported that the mechanism of action in EyeOP1 is similar to other cyclodestructive procedures such as TSCP. The destruction of ciliary

✉ Kin Sheng Lim
shenglim@gmail.com

[1] Department of Ophthalmology, St Thomas' Hospital, London SE1 7EH, UK

[2] King's College London, London SE1 7EH, UK

processes suppresses aqueous humour production which leads to a reduction in IOP [13, 14].

There may be other mechanisms of action contributing to the reduction in IOP as there have been reports of possible changes in uveo-scleral outflow following treatment [15, 16]. We have recently reported the findings of aqueous humour dynamics changes at 3 months' post-HiFU treatment [17]. We showed that the only parameter affected was the aqueous flow rate. The aqueous dynamics parameters can change with time, particularly with the potential modification effect of post-operative inflammation and steroid use. Therefore, we repeated the aqueous humour dynamics measurements on the same cohort of patients at 12 months to assess the long-term effect on aqueous production and outflows following HiFU treatment.

Materials and methods

Patient recruitment

This study was approved by the National Health Service research ethics community, United Kingdom and was registered at clinicaltrials.gov (NCT02839590). Consecutive patients with open angle glaucoma (OAG) or ocular hypertension (OHT) with inadequate IOP control and/or visual field progression on maximally tolerated medical treatment/compliance issues who required further IOP reduction were invited to participate in the study. We have already reported the 3-month result of the study. In the current paper, we present the 12-month follow up results. The recruitment was initiated in August 2016 and completed in January 2017. All patients were provided with an information leaflet upon initial contact. A signed consent was obtained before any measurements or treatment was carried out. This study conformed with the tenets of the Declaration of Helsinki.

Eligibility criteria

All of the following inclusion criteria were met:

All patients between the aged of 18 and 90 years. The upper age limit was chosen to ensure that patients would be able to attend extra appointments for the research purpose.

Diagnosis of OAG or OHT with inadequate IOP control despite maximum medical treatment and/or visual field progression

Ability to undergo accurate fluorophotometry and tonography. Patients were asked if they were able to comfortably lie flat and if they had any postural issues which may restrict their ability to undergo testing.

Patients were excluded if they had any of the following:

Mental impairment conflicting with informed consent or follow-up

Allergy to fluorescein

Any secondary glaucoma

Use of systemic medication such as beta blockers

Current use of any investigational drug, device or current participation in an interventional clinical trial

Previous intraocular incisional surgeries including iridotomies, cataract surgeries or glaucoma filtration surgery

Previous SLT less than 6 months prior to recruitment

Detailed ophthalmic examination

Patients underwent a comprehensive ophthalmic examination which included: visual acuity (ETDRS chart), slit lamp examination, gonioscopy (using two-mirror Magnaview, Ocular Inc. Bellevue, WA, USA), anterior chamber depth and axial length measurements (IOL Master, Carl Zeiss Meditec Inc, Dublin, CA), central corneal thickness (CCT; Pachmate DGH 55, DGH Technology INC, Exton PA), visual field testing (Humphrey automated white on white, 24-1 SITA-standard Carl Zeiss Meditec), and dilated ophthalmoscopy. A 28-day washout from all glaucoma medications was started from the screening visit prior to baseline study measurements (patients attended a 2-week safety visit following the start of washout).

Washout was repeated at 12 months prior to study measurements. Patients remained under observation for routine visits following their 3-month visit. They had tailored treatment plans based on their glaucoma status.

Aqueous dynamics studies

Patients self-administered 3 drops of fluorescein sodium 2% (Minims; Bausch & Lomb, Kingston-upon-Thames, UK) on the night before the baseline study visit (at 22:00) topically into both eyes at 5 min intervals. Patients were given a leaflet outlining the number of drops and the timings to apply the drops. They received a phone call reminder to take their fluorescein drops on the evening prior to their study visit. Fluorophotometry was performed in both eyes with a scanning ocular fluorophotometer between 09:00 am and 12:00 pm (FM-2, Fluorotron Master ocular fluorophotometer; OcuMetrics, Mountain View, CA, USA). Aqueous humour flow rate was determined using a dedicated software provided with the fluorophotometer. Triplicate scans were collected and repeated at 1-h intervals for four measurements to determine the aqueous flow rate (Ft). Pneumatonometry was used to measure IOP following each set of scans (Model 30 Classic; Reichert Ophthalmic Instruments, Depew, NY). The fluorophotometry depends on the equilibrium of fluorescein concentration in the corneal stroma and anterior chamber. Applying additional fluorescein for Goldmann applanation tonometry will disrupt this balance and subsequently fluorophotometry. IOP

was recorded as the mean of 12 measurements per eye with 3 measurements every hour alternating between the two eyes.

Tonographic outflow facility (*C*) was measured by constant weight tonography (5.5–10 g) using a modified digital Schiøtz tonographer (designed by the Department of Bioengineering, Imperial College London, London, UK) between 10:00 and 11:00 am. Our device used an original Schiøtz tonographer footplate from a commercially available unit (model 720, Berkeley Bioengineering Inc., San Leandro, CA, USA) attached to a 3D printed shell that was designed such that the weight conformed to the standards set out by the Committee on Standardization of Tonometers [18, 19]. Displacement of the weighted plunger was measured using a linear variable differential transformer (LVDT; MHR, TE Connectivity, Schaffhausen, CH, USA) driven by a signal conditioner (AD698, Analog Devices, Norwood, MA, USA) and captured digitally by a data acquisition system (USB-6009, National Instruments, Austen, TX, USA). Validation studies confirmed that the LVDT voltage output was linear with respect to the Schiøtz scale reading where each scale reading is equivalent to 0.05 mm of plunger displacement [18, 19]. The procedure was repeated on the contralateral eye after 10 min, whilst the other eye was patched to prevent the corneal surface from drying out.

As the non-invasive clinical measurement of uveoscleral outflow in humans is not possible [20], it is calculated using Goldmann's equation. As part of the equation, we included estimated episcleral venous pressure (EVP) with a range of 10 mmHg based on previous studies by Sit et al. [21].

"*Ff*" is the rate of aqueous humour formation measured by fluorophotometry, "*C*" is the tonographic facility of outflow, "*Pi*" is the IOP, "*Pe*" is the EVP, and "*Fu*" is uveoscleral flow.

$$Ff = (Pi - Pe)C + Fu.$$

Therefore

$$Fu = Ff - C(Pi - Pe).$$

HiFU treatment

There are three different probe sizes available to account for differences in the ocular anatomy. A nomogram has been developed to facilitate white-to-white measurement to calculate the appropriate probe size using optical biometry performed at the baseline visit.

A coupling device is placed on the eye. This ensures the centration and distance from the eye is maintained throughout the procedure. At the base of the probe there is a suction cup to create low level vacuum (225 mmHg) to stabilise the cup on the eye. The 4-ml cavity that is created between the eye, cone and treatment probe is filled with sterile saline solution at room temperature (BSS, Alcon Inc., Fort Worth, TX, USA, or equivalent product). The six elliptical cylinder-shaped impacts are centred on an 11–13 mm diameter circle, depending on the ring diameter chosen, and spread over the eye circumference, while avoiding the nasal–temporal meridian. We used a second-generation probe which differs from the original in its broader active transducer area and more precise temperature calibration of each individual transducer. Patients received 6 s of HIFU treatment.

All HiFU procedures were performed by a single experienced glaucoma surgeon (KSL) under peribulbar anaesthesia (a mixture of lidocaine 2% and levobuprocaine 7.5%). Post-operatively, patients were treated topically with dexamethasone 0.1% preservative free 2 hourly for 2 weeks and then four times per day for 2 weeks. All ocular hypotensive medications were stopped immediately postoperatively.

Postoperative visits

Study visits were at 1 week, 1 month, 3 months and 12 months postoperatively and patients were seen for additional routine visits as judged by the treating clinician. Ocular hypotensive medication could be resumed at the discretion of the treating clinician, but they were all stopped for 28 days prior to the 12-month aqueous humour dynamic measurements (alongside a 2 week safety check to ensure IOP was not dangerously high following washout).

Only one eye treated with HiFU (classified as the worse eye affected by glaucoma/OHT) per participant was included in the data analysis.

The contralateral eye was used as control.

The primary outcome measures were as listed below:

- Intraocular pressure (IOP)
- Facility of tonographic outflow (measured by digital Schiøtz tonometry)
- Aqueous flow rate (measured by fluorophotometry)
- Uveoscleral outflow (calculated from the Goldmann's equation)

These parameters were measured at baseline and at 12 months following a 28-day washout prior to the measurements.

Statistical analyses

Histograms and Shapiro-Wilk test were performed to test for the normality of distribution of data. A Shapiro-Wilk $W > 0.05$ was evidence of normal distribution. Student's paired *t* test was used to compare continuous variables among

groups. When data did not follow normality, non-parametric methods of analysis (Mann–Whitney U and Kruskal-Wallis tests) were used. Pearson's correlation coefficient analysis was used to determine the association of one parameter versus another parameter of aqueous humour dynamics. $P < 0.05$ was considered statistically significant (all analyses, SPSS 24.0; SPSS, Chicago, IL).

Results

Thirty patients were originally recruited to the study. Six patients required further intraocular surgery due to failed treatment (3 patients underwent phacoemulsification + endoscopic cyclophotocoagulation, 2 patient underwent trabeculectomy, 1 patient underwent phacoemulsication + _viscocanalostomy) and 2 patients required phacoemulsifcation surgery due to poor vision. 6 patients were lost to follow up (1 patients was undertaking chemotherapy, 2 patients did not wish to undergo ADS study measurements, 1 patient was unable to undergo washout safely, 1 patient wished to be discharged to the community for follow up and 1 patient were lost to follow up as they moved out of the region) 16 patients met the eligibility criteria at 12 months and were included in the analysis. The contralateral eyes of the recruited patients which received no surgical intervention formed the control group. Sixteen eyes in the treatment group had diagnosis of OAG, whereas 12 eyes in the control group had OAG diagnosis and 4 patients had a diagnosis of OHT. Mean age of the patients in the treatment group was 63.1 ± 11 year-old, there were 9 female and 7 male patients at 12 months follow-up. The majority of patients ($n = 11$) were African/Caribbean. Five patients had prior Selective Laser Trabeculoplasty with the most recent case being 12 months prior (2015, 2015, 2014, 2014, and 2012). Best corrected visual acuity was better in the control eyes (55.7 ± 1.9 vs 51.9 ± 5.4, $p = 0.5$). The baseline characteristics are shown in Table 1.

At baseline, the mean post washout IOP was 28.3 ± 5.7 mmHg. The mean number of medications prior to washout was 3.2 ± 0.7 (median of 3). There was a statistically significant difference in IOP measurement between the treated and control groups at baseline ($p = 0.02$). The baseline aqueous humour dynamics measurements are shown in Table 2.

Primary outcome measures

As aqueous production rate measurement using the fluorophotometric technique can only be accurately performed in eyes with no previous intraocular/incisional surgeries [22], we were only able to enrol 16 patients who have not had any intraocular surgeries at 12 months. In these eyes, the mean post washout IOP was reduced by 21% (28.3 ± 5.7 at baseline vs 22.4 ± 8.4 mmHg at 12 months, $p = 0.04$). Aqueous humour flow rate was reduced by 16% at 12 months' time post HiFU treatment (2.40 ± 0.6 at baseline vs 2.02 ± 0.6 µl/min at 12 months, $p = 0.0493$). There was no statistically significant change in the tonographic outflow facility (TOF) ($p = 0.4$) or uveoscleral outflow ($p = 0.2$). These results are shown in Table 3.

In control eyes, we did not observe any significant difference in the IOP ($p = 0.50$) from baseline compared with 12 months. All aqueous humour parameters remained unchanged at 12 months: aqueous humour flow rate 1.90 ± 0.7 vs 1.40 ± 0.4 µl/min, $p = 0.2$, Tonographic outflow 0.16 ± 0.07 at baseline vs 0.16 ± 0.8 µl/min/mmHg at 12 months, $p = 0.9$ and uveoscleral outflow −0.3 ± 0.99 at baseline vs −0.4 ± 0.9 µl/min at 12 months, $p = 0.6$. These values are shown in Table 4. There were no treatment-related complications in any of the 16 patients.

Table 1 Baseline characteristics of treated and control eyes.

	Treated eyes ($n = 16$)	Control eyes ($n = 16$)	*P* value	95% CI
Age, years	63.1 ± 11	63.7 ± 11	0.9	−8.7–9.1
Race (Black: White)	11:5	11:5	—	—
Diagnosis (OHT:POAG)	0:16	4:12	—	—
Gender (F:M)	9:7	9:7	—	—
BCVA	51.9 ± 5.4	55.7 ± 1.9	0.5	−5.3–0.4
CCT, µm	528.6 ± 42	526 ± 43	0.4	−8.5–44.0
ACD, mm	3.21 ± 0.3	3.26 ± 3.5	0.6	−0.1–0.3
AXL, mm	24.0 ± 1.2	23.9 ± 0.9	0.3	−0.8–0.7
WTW, mm	11.9 ± 0.3	11.8 ± 0.4	0.1	−0.3–0.1
Number of meds	3.2 ± 0.7 (median = 3)	2.6 ± 1.2 (median = 3)	0.1	−0.1–0.9
MD, dB	−12.3 ± 7.1	−6.9 ± 8.2	**<0.05**	−11.7– −3.6

OHT ocular hypertension, *POAG* primary open angle glaucoma, *CCT* central corneal thickness, *ACD* anterior chamber depth, *AXL* axial length, *WTW* white-to-white, *MD* Mean deviation.

Discussion

In this study, we assessed the change in aqueous humour dynamics at 12 months after the initial HiFU treatment. Sixteen patients with previously uncontrolled IOP despite maximal medical therapy who received HiFU treatment were included. They had undergone aqueous dynamics measurements at baseline and at 12 months post treatment. These measurements were performed after the 28-day of washout at baseline and at the 12-month visit. Our results showed a statistically significant reduction in IOP and aqueous humour

Table 2 Aqueous humour dynamics measurements at baseline and 12 months' time in treatment and control groups.

	Treated eyes ($n = 16$)	Control eyes ($n = 16$)	P value
Baseline IOP (mmHg)	28.3 ± 5.7	23.4 ± 7.4	0.02
Baseline aqueous flow rate (µl/min)	2.4 ± 0.6	1.88 ± 0.7	0.3
Baseline Tonographic Outflow Facility (µl/min/mmHg)	0.12 ± 0.9	0.16 ± 0.1	0.5
Baseline Uveoscleral outflow (µl/min)	0.6 ± 1.25	−0.25 ± 0.99	0.5

Student's paired T test results.

Table 3 Aqueous humour dynamics and IOP measurements in treatment group at baseline and twelve months post operatively.

	Baseline ($n = 16$)	12 months post operatively ($n = 16$)	% Change	P value
IOP (mmHg)	28.3 ± 5.7	22.4 ± 8.4	21%	0.04[a]
Aqueous flow rate (µl/min)	2.40 ± 0.6	2.02 ± 0.6	16%	0.0493[b,a]
Tonographic outflow facility (µl/min/mmHg)	0.12 ± 0.09	0.08 ± 0.05	NA	0.4
Uveoscleral outflow (µl/min)	0.6 ± 1.3	1.3 ± 0.85	NA	0.2

Student's paired t test results.

[a]Statistical significance.

[b]Wilcoxson signed ranked test.

Table 4 Aqueous humour dynamics measurements in control group at baseline and twelve months follow up.

	Baseline ($n = 16$)	12 months ($n = 16$)	P value
IOP (mmHg)	23.4 ± 7.4	22.2 ± 7.4	0.5
Aqueous flow rate (µl/min)	1.9 ± 0.7	1.4 ± 0.4	0.2
Tonographic outflow facility (µl/min/mmHg)	0.16 ± 0.7	0.16 ± 0.8	0.9
Uveoscleral outflow (µl/min)	−0.3 ± 0.99	−0.4 ± 0.9	0.6

Student's paired t test.

flow rate. IOP was reduced by 21% and aqueous humour flow rate was reduced by 16% at 12-months' time post HiFU treatment, in those eyes that remained in the study. Aqueous humour flow rate reduction following HiFU treatment due to the cyclodestruction of ciliary epithelium is likely to be related to the significant IOP reduction [15]. We demonstrated that the effect of a single HiFU application can last up to 12 months. We did not observe significant change in the TOF or uveoscleral outflow. In aqueous dynamic studies, TOF is generally considered to be the surrogate for trabecular outflow facility.

There are limited published clinical studies that analyse the aqueous humour dynamics in human eyes following a cyclodestructive procedure. Traditionally, cyclodestructive treatment methods are used to treat refractory glaucoma cases due to the associated high rates of complications [11], such as reduced visual acuity, inflammation and phthisis bulbi. The coagulation necrosis of the ciliary body has been reported to be more selective and with a lower rate of complications compared to the traditional diode laser [23]. In our series, there were no postoperative complications. A recent study by Marques et al. [24] showed a risk of increased corneal astigmatism associated with HiFU but it had no significant impact on overall refraction. The primary mechanism of action of HiFU is the destruction of the ciliary epithelium. In our previous study [17], we demonstrated that IOP reduction was due to reduced aqueous flow rate at 3 months. The uveoscleral outflow and TOF remained unchanged [17]. Some researchers have hypothesised other possible adjunctive mechanisms of action including flow through the sclera [15], as well as inducing stimulation of the suprachoroidal and transscleral portions of the uveoscleral outflow pathway [25, 26].

Aptel et al. [13] treated rabbits' eyes ($n = 18$) with HiFU. They specifically evaluated histological changes of ciliary bodies. Their results showed a 55% reduction in IOP, 4 weeks after treatment which was attributed to the destruction of the bi-layered ciliary body epithelium. The authors described coagulation necrosis lesions within the ciliary body processes with loss of the epithelium, stromal oedema and vascular congestion. No evidence of scleral thinning or significant inflammation was identified. Our

study findings in humans support the above laboratory findings of a reduction in the aqueous flow rate in the short-term. A following study by the same authors with an increased number of rabbits ($n = 34$) utilising light and electron microscopy showed that there may be a dual effect on aqueous humour dynamics [27] for up to 6 months. In addition to the thermal destruction of the ciliary process epithelium, there was also a sustained fluid space seen between the sclera, ciliary body and the choroid indicating an increase in outflow by the uveoscleral pathway.

Long-term scleral thinning in the majority of rabbit eyes was observed and these changes were maintained for up to six months. The authors speculated that this was due to tissue retraction or tissue micro-architectural changes rather than intraocular inflammation [27]. Studies in monkeys demonstrated an increase in uveoscleral outflow following diode laser treatment applied to the pars plana portion of the ciliary body [28, 29]. However, our clinical study did not support those findings as there was no detectable change in the uveoscleral outflow following HiFU treatment at 1 year.

Clinical studies in humans have shown a reduction in IOP between 25 and 38% [10, 30–32] but these studies did not include a washout period. Whilst our study only included OAG patients, the previous studies have had a range of glaucoma diagnoses. Mastropasqua et al. [15] demonstrated that HiFU induced anatomical modifications of the sclera and conjunctiva and suggested that transscleral aqueous humour outflow enhancement was a possible mechanism alongside decreased aqueous production for reducing IOP. The results from our study however failed to support this hypothesis as we did not find any statistically significant change in the uveoscleral and trabecular outflow 12 months after treatment.

It is important to stress that this study cannot comment of the success rate and the IOP reduction post HiFU treatment at 12 months. This is an observational study investigating the mechanism of IOP reduction following HiFU in those eyes that remained in the study at 12 months. Compared to our previous report of the 3-month results post HiFU treatment [17], the reduction of IOP (16% at three months and 21% at twelve months) in those 'treatment success' eyes, could be explained by the reduction in aqueous humour flow rate (15% at three months and 16% at twelve months) alone. There was no significant change in the tonographic (trabecular) outflow facility and the calculated uveoscleral outflow at 3 and 12 months. 12 month results have been recently reported by Marques et al. in a prospective pragmatic study showing a 34% reduction in IOP and 1 year surgical success rate of 71.4% [33].

One of the main limitations of our study has been the high attrition rate of patients during the follow up. Nonetheless, our results showed corresponding IOP reduction and aqueous flow rate reduction at 12 months, suggesting that despite the passage of time, the mechanism of action remained the same at 12 months. However, a larger sample size could have strengthened the findings and discussion. Our patients only received one application of treatment. This is unlike other studies in which patients had retreatment if IOP was not sufficiently controlled following one procedure. Aptel et al. [34] showed repeated treatment could be considered safe and effective following early or delayed failure after the original treatment. Our study excluded pseudophakic patients as it is not possible to carry out fluorophotometry in this cohort. There may be a difference in the efficacy of HiFU in phakic and pseudophakic eyes. Our results may not be generalisable to other types of cyclodestructive treatments such as cyclodiode laser, due to the potential different mechanism of action and the significantly high proportion of African/Caribbean patients. At 12 months following HiFU treatment, reduction in IOP is proportional to the reduction in aqueous flow rate with no detectable change in uveoscleral outflow or TOF.

Summary

What was known before

- What was known before: HIFU has been shown to be effective in the treatment of glaucoma. The reduction of IOP in the early stages has been shown to be due to reduced aqueous humour flow rate.

What this study adds

- What this study adds: Longer term data showing that the reduction in aqueous humour flow rate is unchanged at 12 months There is no change to other outflow pathways.

Funding Unrestricted funding from EyeTechCare.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma

burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121:2081–90.
2. Gaasterland DE, Ederer F, Beck A, Costarides A, Leef D, Closek J, et al. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. Am J Ophthalmol. 2000;130:429–40.
3. Miglior S, Bertuzzi F. Relationship between intraocular pressure and glaucoma onset and progression. Curr Opin Pharmacol. 2013;13:32–35.
4. Fankhauser F, Kwasniewska S, Van Der Zypen E. Cyclodestructive procedures - I. Clinical and morphological aspects: a review. Ophthalmologica. 2004;218:77–95.
5. Dastiridou AI, Katsanos A, Denis P, Francis BA, Mikropoulos DG, Teus MA, et al. cyclodestructive procedures in glaucoma: a review of current and emerging options. Adv Ther. 2018;35:2103–27.
6. Michelessi M, Bicket AK, Lindsley K. Cyclodestructive procedures for non-refractory glaucoma. Cochrane Database Syst. Rev. 2018;4:CD009313.
7. Kosoko O, Gaasterland DE, Pollack IP, Enger CL. Long-term outcome of initial ciliary ablation with contact diode laser transscleral cyclophotocoagulation for severe glaucoma. Ophthalmology. 1996;103:1294–302.
8. Posarelli C, Covello G, Bendinelli A, Fogagnolo P, Nardi M, Figus M. High-intensity focused ultrasound procedure: the rise of a new noninvasive glaucoma procedure and its possible future applications. Surv Ophthalmol 2019;64:826–34.
9. Mastropasqua R, Fasanella V, Mastropasqua A, Ciancaglini M, Agnifili L. High-intensity focused ultrasound circular cyclocoagulation in glaucoma: a step forward for cyclodestruction? J Ophthalmol. 2017;2017:14.
10. Giannaccare G, Vagge A, Sebastiani S, Urbini LE, Corazza P, Pellegrini M, et al. Ultrasound cyclo-plasty in patients with glaucoma: 1-year results from a multicentre prospective study. Ophthalmic Res. 2019;61:137–42.
11. Melamed S, Goldenfeld M, Cotlear D, Skaat A, Moroz I. High-intensity focused ultrasound treatment in refractory glaucoma patients: Results at 1 year of prospective clinical study. Eur J Ophthalmol. 2015;25:483–9.
12. Charrel T, Aptel F, Birer A, Chavrier F, Romano F, Chapelon JY, et al. Development of a miniaturized HIFU device for glaucoma treatment with conformal coagulation of the ciliary bodies. Ultrasound Med Biol. 2011;37:742–54.
13. Aptel F, Charrel T, Palazzi X, Chapelon JY, Denis P, Lafon C. Histologic effects of a new device for High-Intensity focused Ultrasound Cyclocoagulation. Investig. Ophthalmol Vis Sci. 2010;51:5092–8.
14. Denis P, Aptel F, Rouland JF, Nordmann JP, Lachkar Y, Renard JP, et al. Cyclocoagulation of the ciliary bodies by high-intensity focused ultrasound: a 12-month multicenter study. Investig Ophthalmol Vis Sci. 2015;56:1089–96.
15. Mastropasqua R, Agnifili L, Fasanella V, Toto L, Brescia L, DI Staso S, et al. Uveo-scleral outflow pathways after ultrasonic cyclocoagulation in refractory glaucoma: an anterior segment optical coherence tomography and in vivo confocal study. Br J Ophthalmol. 2016;100:1668–75.
16. Coleman DJ, Silverman RH, Ursea R, Rondeau MJ, Lizzi FL. Ultrasonically induced hyperthermia for adjunctive treatment of intraocular malignant melanoma. Retina. 1997;17:109–17.
17. Alaghband P, Galvis E, Ramirez A, Madekurozwa M, Chu B, Overby D, et al. The effect of high-intensity focused ultrasound on aqueous humor dynamics in patients with glaucoma. Ophthalmol Glaucoma. 2020;3:122–9.
18. Friedenwald JS Standardization of tonometers: Decennial report by the Committee on Standardization of Tonometers. In: American Academy of Ophthalmology and Otolaryngology.; 1954. pp. 266–72.
19. Alaghband P, Baneke A, Galvis E, Madekurozwa M, Chu B, Overby D, et al. Aqueous humor dynamics in uveitis: A comparative study in hypertensive uveitis. Investig Ophthalmol Vis Sci. 2017;208:347–55.
20. Johnson M, McLaren JW, Overby DR. Unconventional aqueous humor outflow: a review. Exp Eye Res. 2017;158:94–111.
21. Sit AJ, McLaren JW. Measurement of episcleral venous pressure. Exp Eye Res. 2011;93:291–8.
22. Brubaker RF, McLaren JW. Uses of fluorophotometry in glaucoma research. Ophthalmology. 1985;92:884–90.
23. Graber M, Rothschild PR, Khoueir Z, Bluwol E, Benhatchi N, Lachkar Y. High intensity focused ultrasound cyclodestruction versus cyclodiode treatment of refractory glaucoma: a retrospective comparative study. J Fr Ophtalmol. 2018;41:611–8.
24. Marques RE, Sousa DC, Vandewalle E, Somers A, Melamed S, Nardi M, et al. The effect of glaucoma treatment using high-intensity focused ultrasound on total and corneal astigmatism: a prospective multicentre study. Acta Ophthalmol. 2020. https://doi.org/10.1111/aos.14467. Online ahead of print.
25. Denis P, Aptel F, Rouland JF, Nordmann JP, Lachkar Y, Renard JP, et al. Cyclocoagulation of the ciliary bodies by high-intensity focused ultrasound: a 12-month multicenter study. Investig Ophthalmol Vis Sci. 2015;56:1089–96.
26. Aptel F, Lafon C. Treatment of glaucoma with high intensity focused ultrasound. Int J Hyperth. 2015;31:292–301.
27. Aptel F, Béglé A, Razavi A, Romano F, Charrel T, Chapelon JY, et al. Short- and long-term effects on the ciliary body and the aqueous outflow pathways of high-intensity focused ultrasound cyclocoagulation. Ultrasound Med Biol. 2014;40:2096–106.
28. Liu GJ, Mizukawa A, Okisaka S. Mechanism of intraocular pressure decrease after contact transscleral continuous-wave Nd:YAG laser cyclophotocoagulation. Ophthalmic Res. 1994;26:65–79.
29. Ho CL, Wong EYM, Chew PTK. Effect of diode laser contact transscleral pars plana photocoagulation on intraocular pressure in glaucoma. Clin Exp Ophthalmol. 2002;30:343–7.
30. Aptel F, Denis P, Rouland J, Nordmann J, Lachkar Y, Renard J, et al. Ultrasonic circular cyclo coagulation in patients with primary open-angle glaucoma: a multicenter clinical trial. Acta Ophthalmol. 2013;91:252–8.
31. Aptel F, Denis P, Rouland JF, Renard JP, Bron A. Multicenter clinical trial of high-intensity focused ultrasound treatment in glaucoma patients without previous filtering surgery. Acta Ophthalmol. 2016;94:268–77.
32. Ye C, Wang XY, Bian XQ, Liang YB. High-intensity focused ultrasound in the treatment of glaucoma. Zhonghua Yan Ke Za Zhi 2020;56:66–70.
33. Marques RE, Ferreira NP, Sousa DC, Barata AD, Sens P, Marques-Neves C, et al. High intensity focused ultrasound for glaucoma: 1-year results from a prospective pragmatic study. Eye. 2020. https://pubmed.ncbi.nlm.nih.gov/32317796/ (Accessed October 21, 2020).
34. Aptel F, Tadjine M, Rouland JF. Efficacy and safety of repeated ultrasound cycloplasty procedures in patients with early or delayed failure after a first procedure. J Glaucoma. 2020;29:24–30. https://doi.org/10.1097/IJG.0000000000001400.