Malaysian Journal of Ophthalmology

© Malaysian Journal of Ophthalmology 2022; 4:262-271
Case series
https://doi.org/10.35119/myjo.v4i3.248

Ultrasound cycloplasty: a case series examining the efficacy on a local Malaysian cohort of patients

Shankari **Sothirachagan**, Jemaima **Che Hamzah**

[1]*Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia*

Abstract

Introduction: Ultrasound cycloplasty (UCP) is commercially available in Europe. It has been shown to have less side effects than its trans-scleral diode laser cyclophotocoagulation counterpart in reducing intraocular pressure (IOP) in refractory glaucoma patients.
Case presentation: This retrospective case series followed seven patients treated with UCP for refractory glaucoma at the Ophthalmology Clinic, Hospital Universiti Kebangsaan Malaysia. Patients were aged 52–80 years, with baseline IOP 14–27 mmHg. All patients received sequential activation of the transducers lasting 8 seconds. Postoperatively, patients were followed-up at 1 week, 1 month, and 3 months. No complications or changes in best-corrected visual acuity were recorded postoperatively. One patient underwent a trabeculectomy 3 months post-procedure, whilst the others continued regular medication.
At 1-month postoperative, there was IOP reduction of 6–10 mmHg in six patients. At the 3-month follow-up, IOP returned to the preoperative levels. Conservative power and duration of the shots were used to ensure patients safety.
Conclusion: Most studies on UCP safety and efficacy have been conducted on Caucasian populations. A longer duration of UCP may be necessary in the Asian population. Further studies are required to determine the efficacy of UCP in the Asian population.

Keywords: Malaysia, refractory glaucoma, ultrasound cycloplasty

Correspondence: Jemaima Che Hamzah, PhD, Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, 9th floor, Clinical Block, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur, Malaysia.
E-mail: jemaima@ppukm.ukm.edu.my

Sikloplasti ultrasound: kajian kes siri ke atas efikasi dikalangan pesakit setempat di Malaysia

Abstrak

Pengenalan: Kaedah baru siklokoagulasi ultrasonic (UCP) terdapat di pasaran komersil di Eropah.. Menurut kajian, kaedah ini mempunyai kesan sampingan yang lebih rendah berbanding kaedah laser diode trans-skleral siklofotokoagulasi dalam pengurangan tekanan intraocular (IOP) bagi pesakit glaukoma refraktori.
Pembentangan kes: Satu kajian retrospektif kes bersiri dijalankan atas tujuh pesakit dengan glaukoma refraktori di Klinik Oftalmologi, Pusat Perubatan Universiti Kebangsaan Malaysia. Kesemua pesakit terlibat berumur di antara 52 dan 80 tahun dengan IOP 14-27mmHg. Mereka menerima pengaktifan transduser berturutan selama 8 saat. Selepas prosedur ini, temujanji rawatan susulan teleh diberikan selepas seminggu, sebulan dan 3 bulan. Didapati tiada perubahan dalam ketajaman penglihatan terbaik (BCVA) dan tiada komplikasi dicatatkan sepanjang temujanji selepas prosedur. Hanya seorang pesakit perlu menjalani pembedahan trabekulektomi tiga bulan selepas prosedur, manakala yang lain meneruskan rawatan yang ditetapkan. Sebulan selepas pembedahan, enam pesakit menunjukkan penurunan IOP sebanyak 6-10mmHg. Walau bagaimanapun, pada rawatan susulan bulan ketiga, IOP kembali ke paras sebelum prosedur. Bagi melindungi pesakit, hanya kuasa laser dan jangka masa yang konservatif diaplikasikan ke atas pesakit.
Kesimpulan: Kebanyakkan hasil kajian menunjukkan kaedah ini adalah efektif dan selamat dalam menurunkan IOP dengan kesan sampingan yang mínima di kalangan pesakit orang kulit putih. Pesakit dari populasi Asia mungkin memerlukan durasi prosedur yang lebih lama. Kajian yang lebih mendalam diperlukan untuk menilai keberkesanan UCP bagi populasi Asia.

Kata kunci: glaukoma refraktori, Malaysia, sikloplasti ultrasound

Introduction

Glaucoma is one of the leading causes of blindness in the world and it is estimated to reach 76 million cases worldwide in 2020, and to increase to 111 million cases by 2040.[1,2] The main risk factor, although not exclusive, is an elevated intraocular pressure (IOP). IOP reduction is currently the only treatment that has been proven effective in slowing down the progression of glaucoma.[2,3] Medical treatment is considered the first-line therapy, whilst the gold-standard surgical approach, trabeculectomy, is typically reserved for advanced, drug-intolerant cases.

In refractory glaucoma, destruction of the ciliary body (CB) is considered the treatment of last resort to control IOP. The coagulation techniques that decrease aqueous humour (AQH) production use a variety of energy sources including laser, microwave, cryotherapy, and ultrasound.[2,3] As cyclodestruction is associated with several disadvantages, it is considered an end-stage procedure.

Trans-scleral diode laser cyclophotocoagulation (TSCPC) is the most applied cyclodestructive procedure,[3,4] although it is associated with side effects such as chronic uveitis, hypotony, and serous retinal detachment.[2,4,5] In the last decades, high-intensity focused ultrasound (HIFU) has been studied as a cyclodestructive procedure.[2,3] This method causes a transient hyperthermia focused on the desired area of the CB, sparing damage to the surrounding tissue.[2,3]After a series of successful clinical trials in Europe, ultrasound cycloplasty (UCP) was approved for the treatment of refractory glaucoma and made commercially available. The aim of this study was to determine the efficacy of UCP on our cohort of refractory glaucoma patients.

Case presentation

Methods

This is a retrospective case series conducted on seven patients recruited from the Ophthalmology Clinic at Hospital Universiti Kebangsaan Malaysia. Patients were included in the study if they were > 18 years, had refractory glaucoma on maximum topical antiglaucoma therapy, and had evidence of glaucoma progression. Patients who had surgical and laser intervention in the 3 months prior to surgery or previous CB ablation were excluded.

At baseline, patients underwent best-corrected visual acuity (BCVA), slit lamp microscopy examination, Goldmann applanation tonometry, fundus examination with 78 D or 90 D, biometry, and visual field testing (24-2 and 10-2 full threshold test). Biometry was done as the size of the ultrasound probe is determined by axial length and white-to-white measurements. These measurements determine probe size, as the diameters correspond to the CB focal zones to be targeted. Ocular anatomy presents normal variations, including the limbal-ciliary body distance. To account for these differences, three probe sizes (11, 12 and 13 mm) are commercially available.

The procedure was done under aseptic technique in the operation theatre. Once supine, peribulbar anaesthesia was given. All procedures were conducted by the same surgeon. The coupling cone, connected to a suction ring, was placed directly onto the ocular surface aligned with the optical axis. The ultrasound beam was focused at a 2 mm depth beneath the sclera, which corresponded to the CB. The suction ring kept the cone in direct contact with the eye to prevent ocular movement and misalignment. The space between the eye and the coupling cone/

probe was filled with balanced salt solution. The following parameters were used: suction ring, 70 mmHg; number of sectors activated, six; duration of each of the six shots, 8 seconds; and time between each shot, 20 seconds.

Patient 1 received four sectors, while patients 2–6 received six sectors. Patient 1 had a previous failed trabeculectomy in the affected eye and subsequently opted for UCP treatment instead of a revision of the trabeculectomy. Patients 2–6 were given the option of surgery first but refused.

Patient 3 had ocular hypertension and was the only patient given acetazolamide 250 mg QID until UCP, in addition to maximum topical antiglaucoma medication. He had uncontrolled IOP in his only functioning eye despite good compliance. In this case, systemic medication did not help in IOP reduction, as the patient subsequently required a trabeculectomy.

Postoperatively, patients received gutt prednisolone acetate 1% and ciprofloxacin hydrochloride 0.3% every 2 hours, and neomycin/polymyxin B sulphate and dexamethasone ointment at night for 2 weeks. Medications were tapered gradually over a 2-month period. Preoperative hypotensive medications were unaltered throughout the course of the follow-up. Follow-up was done at 1 week, 1 month, and 3 months. Earlier appointments were given if required.

Results

Table 1 presents the patient demographics, clinical findings, glaucoma diagnosis, and visual field test results. Table 2 presents preoperative and postoperative values at all follow-up points for BCVA and IOP.

The patients who had high IOP on follow-up were managed accordingly with oral and intravenous antiglaucoma medication. Patient 3, who had IOP of 32 mmHg at the 3-month follow-up underwent a trabeculectomy. Patient 6 defaulted the 1-month follow-up and Patient 5 defaulted the 3-month follow-up. No complications were found postoperatively.

Discussion

IOP reduction can be achieved by reducing production or increasing outflow of AQH. The two mechanisms can be modified reversibly via topical and systemic medication, or permanently with laser procedures and surgery[5]. Cyclophotocoagulation (CPC) is the most common cyclodestructive procedure used in clinical practice[5] and involves the destruction of the CB epithelium by coagulative necrosis.

The diode laser (810 nm wavelength) is better absorbed by CB melanin pigment and therefore has more targeted tissue destruction.[5] Generally, TSCPC and endoscopic cyclophotocoagulation (ECP) are indicated for refractory glaucoma,

Table 1. Patient demographics, clinical findings, diagnosis, and visual field test results

P	Demographics (age, ethnicity, sex)	Comorbidities	Diagnosis	Baseline mean VF MD
1	52, Malay, M	ESRF, HTN, hepatitis C, asthma	Advanced POAG	-29.69 dB
2	54, Malay, F	DM, HTN	Advanced POAG	-20.44 dB
3	63, Malay, M	HPL	Ocular hypertension	-0.74 dB
4	73, Chinese, M	HTN, HPL, gout	Advanced POAG	-16.62 dB
5	80, Malay, M	HTN	Advanced POAG	Unable to perform VF
6	75, Chinese, M	HTN, CKD, IHD, stroke, adrenal adenoma	Advanced POAG	-17.54 dB
7	59, Chinese, M	HTN	Angle recession	-23.08 dB

P: patient; ESRF: end-stage renal failure; HTN: hypertension; HPL: hyperlipidaemia; CKD: chronic kidney disease; IHD: ischaemic heart disease, POAG: primary open-angle glaucoma; VF: visual field; MD: mean deviation

Table 2. Preoperative and postoperative best-corrected visual acuity and intraocular pressure

P	Preoperative		Postoperative follow-up					
	BCVA (unaided/ pinhole)	IOP	1 week		1 month		3 months	
			BCVA	IOP	BCVA	IOP	BCVA	IOP
1	6/24 (6/24)	17	6/60 (6/60)	13	6/36 (6/36)	09	6/36 (6/24)	17
2	6/6	17	6/18 (6/9)	11	6/6	16	6/6	18
3	6/9 (6/9)	20	6/12 (6/12)	20	6/12 (6/9)	28	6/12 (6/9)	32*
4	6/12 (6/9)	24	6/18 (6/12)	14	6/18 (6/12)	12	6/18 (6/12)	14
5	CF	27	HM	12	CF	16	-	-
6	6/18 (6/18)	20	6/18 (6/12)	16	-	-	6/18 (6/12)	18
7	3/60	14	3/60	14	3/60	30	3/60	16

P: patient; BCVA: best-corrected visual acuity; IOP: intraocular pressure, HM: hand movement; CF; counting fingers
*Patient underwent trabeculectomy after the 3-month follow-up.

or eyes with significantly compromised visual acuity or poor visual potential.[5] The previous coagulation techniques have two major drawbacks: (i) the inability to deliver focused energy at a specific target organ site, which leads to surrounding tissue damage; and (ii) the unpredictable dose-effect relationship which prevents the titration of the treatment.

UCP is the latest technology to induce CPC, which is applied as a system of minitransducers. There is rapid sequential activation that produces six focused ultrasound beams, which stimulate six segments of linear CB tissue coagulation; these areas undergo focal thermal necrosis.[1] The focused beams allow controlled transmission through optically opaque ocular media[1] and minimise structural damage to adjacent tissue. This technique is faster, simpler, safer, and less invasive than previous methods such as TSCPC and ECP.[2-4]

These features enable UCP to be done as an outpatient procedure. UCP has been found to lower IOP by (i) necrosing CB epithelium, which decreases the AQH production,[1-3] and (ii) stimulating the unconventional drainage pathway via the suprachoroidal and trans-scleral portions of the uveoscleral pathway. Mastropasqua *et al.* observed anatomical changes in the microarchitecture of the sclera.[4] They found an increase in the intrascleral hyporeflective spaces with anterior segment optical coherence tomography and presence of microcysts on histology. Microcysts were initially described in the epithelial wall of the functioning bleb in trabeculectomy as an indicator of transconjunctival AQH filtration.[2,3,6,7]

Minimal surrounding tissue destruction and a smaller ocular surface involvement ensures a faster postoperative recovery.[3] Furthermore, the effect is not dependent on the degree of CB pigmentation.[1] There is less postoperative inflammation; even though the CB epithelium is remodelled, the blood-aqueous barrier remains intact.[4] Other advantages include a better safety profile with less complications, such as persistent hypotony and phthisis bulbi.

The TSCPC approach is essentially a 'blind' procedure, commonly reserved for patients who are unfit for filtering surgery or who refused filtration surgery.[9] There is disruptive tissue damage (microexplosions heard as audible "pops") and tissue ischaemia.[9] These can lead to complications such as anterior chamber inflammation (due to blood-aqueous barrier breakdown), hyphaema, hypotony, cataract progression, and rarely, sympathetic ophthalmia.[5,9] Although TSCPC has been used successfully to reduce IOP in patients with advanced glaucoma, the thermal damage to surrounding tissues and associated complications have resulted in TSCPC being used as a last resort in refractory glaucoma.[9]

Subsequently, transpupillary CPC allowed direct visualisation of the CB. Unfortunately, the clear visual axis and dilated pupil requirement along with unpredictable postoperative outcomes[10-12] made it unpopular amongst surgeons.

ECP, a newer CPC technique, enabled the CB epithelium to be accessed via a limbal or pars plana approach. The former is proposed in patients with pre-existing cataract and is planned to receive combined ECP and cataract removal with

intraocular lens implantation surgery. The pas plana approach is commonly reserved for pseudophakic patients and provides the most inclusive view of the ciliary processes. Anterior vitrectomy is performed in this approach. ECP is reported to be superior to TSCPC because: (i) it allows better visualisation of the ciliary processes; (ii) cyclodestruction can be delivered in a targeted manner, minimising collateral tissue damage; and (iii) the laser can be delivered in a highly titratable manner. To date, there are no long-term randomised prospective studies comparing ECP to TSCPC and trabeculectomy.[6,13] The risks of ECP combined with cataract surgery include hypotony, ciliary block glaucoma, and phthisis bulbi.[7,13] As ECP is an invasive procedure, it can be complicated by postoperative infections.[8] Variable postoperative refractive outcomes may occur with an ECP combined surgery.[8] More myopic shifts were reported in eyes with angle closure after a combined operation.[8,14] Postoperative inflammation has been suggested to be more intense after a combined ECP procedure than when performed alone.[8] Surgeons must also be extremely selective when performing a combined operation to minimise the risk of cystoid macular oedema.

To our knowledge, we are the first to conduct UCP in Malaysia. Prior to the procedure, all patients had an IOP of < 30 mmHg and were on at least three, if not maximum, topical antiglaucoma medications. No changes in visual acuity occurred postoperatively. At the 1-week and 1-month follow-up, an IOP reduction of 6–10 mmHg was noted in six patients. However, by the 3-month follow-up, the IOP had returned to preoperative levels. There may be several reasons for this. To ensure the safety of this procedure in our patients, we used a conservative power and duration of the shots, based on protocols defined in studies performed on Caucasian populations. As our cohort of patients are of an Asian origin, a higher power and longer duration may be required to achieve the same outcome as in those studies.

Several limitations were identified. This case series consists of small number of patients with preoperative IOP < 30 mmHg. Giannacare *et al.* postulated that UCP would be more effective in patients with a higher preoperative IOP. Therefore, a higher preoperative IOP value may result in a bigger IOP reduction. The study also reported that a quarter of patients did not respond to UCP treatment, and an estimated half required subsequent surgery to further control IOP.[15] It may be possible that the selected patients given this treatment were not responsive and may not be a true reflection of the efficacy of UCP. Aptel *et al.* stated that selected patients may be classified as early failures.[14,16] Hypothetical models of failure can be classified into early or late depending on the time of onset.[14,16] Early failures may reflect an insufficient circumferential amount of coagulated ciliary tissue during the procedure, whilst late failures imply possible re-epithelialisation of the ciliary processes with recovery of its function[15] or the gradual reduction of the stimulated unconventional outflow pathway.[14,16]

Insufficient treatment may be possible in our patients. Giannacare *et al* noted an improved efficacy with the 8-second treatment, commonly used in Europe.[15]

Although Deb-Joardar *et al.* found no significant difference between an 8- and 10-second protocol in a cohort of Indian patients, it may be useful for future research to consider a longer duration of 10 seconds instead of the 8 seconds of application in our patients.[2] This may aid in determining if the 10 second protocol is beneficial in our cohort. Furthermore, the number of sectors could be increased from six to eight.

Therefore, re-treatment in our patients may be necessary. Given the nature of UCP, minimal postoperative inflammation and quicker recovery further supports re-treatment. Several studies have sought to evaluate the efficacy and safety of repeated UCP treatments in patients with a previous failed first UCP procedure. Aptel *et al.* found that patients who underwent re-treatment demonstrated good IOP reduction at 1 and 3 months post-repeat procedure. However, only one of the four patients re-treated showed sustained IOP reduction at 1 year post-procedure.[16]

With the recent Covid-19 pandemic, clinics were severely reduced in patient load and many of our patients were reluctant to be reviewed. This made it difficult to follow up patients and to review IOP trends at the established follow-up time points. As mentioned previously, the first 3 postoperative months are critical to classify a patient as a success or failure. The team had to rely on patient claims regarding their compliance to the postoperative topical steroid medication.

Conclusion

UCP has been proven to be effective in IOP reduction with minimal postoperative side effects. The CB epithelium is remodelled while the blood-aqueous barrier remains intact. This not only reduces postoperative inflammation but supports the option of re-treatment, especially in patients where the desired IOP is yet to be achieved. Our series may not have reflected a positive outcome, but it remains a procedure that has been proven to be safer, less invasive, and with a faster recovery period compared to traditional cyclodestructive procedures. Further studies are required to determine the efficacy of UCP in the Asian population.

Declarations

Ethics approval and consent to participate
As a retrospective case series, this study did not require ethics approval.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

References

1. Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta analysis. Ophthalmology. 2014;121:2081 90. https://doi.org/10.1016/j.ophtha.2014.05.013
2. Deb Joardar N, Reddy KP. Application of high intensity focused ultrasound for treatment of open-angle glaucoma in Indian patients. Indian J Ophthalmol. 2018;66:517-23. https://doi.org/10.4103/ijo.IJO_1024_17
3. Mastropasqua R, Agnifili L, Fasanella V, 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(12):1668-1675. https://doi.org/10.1136/bjophthalmol-2015-308069
4. Vernon SA, Koppens JM, Menon GJ, et al. Diode laser cycloablation in adult glaucoma: long-term results of a standard protocol and review of current literature. Clin Exp Ophthalmol. 2006;34:411–20. https://doi.org/10.1111/j.1442-9071.2006.01241.x
5. Aref AA, Jindal AP, Giaconi JO, Eliassi-Rad B. Cyclodestructive Procedures in Treatment of Glaucoma. American Academy of Ophthalmology, Eyewiki. June 2019. Available from: https://eyewiki.aao.org/Cyclodestructive_Procedures_in_Treatment_of_Glaucoma. Accessed March 2021.
6. Pantcheva MB, Kahook MK, Schuman JS, et al. Comparison of acute structural and histopathological changes in human autopsy eyes after endoscopic cyclophotocoagulation and trans-scleral cyclophotocoagulation. Br J Ophthalmol. 2007;91:248–52. https://doi.org/10.1136/bjo.2006.103580
7. Netland PA, Mansberger SL, Lin S. Uncontrolled intraocular pressure after endoscopic cyclophotocoagulation. J Glaucoma. 2007;16:165–167. https://doi.org/10.1097/01.ijg.0000243475.36213.41
8. Glaucoma Today [Internet]. Pennsylvania, BMC. (March/April 2017). [cited August 2021]. A Targeted Approach, Endocyclophotocoagulation for Glaucoma Management. Available from: https://glaucomatoday.com/articles/2017-mar-apr/a-targeted-approach.
9. Dastiridou AI, Katsanos A, Denis P, et al. Cyclodestructive Procedures in Glaucoma: A Review of Current and Emerging Options. Adv Ther. 2018;35:2103–2127. https://doi.org/10.1007/s12325-018-0837-3.
10. Lee PF. Argon laser photocoagulation of the ciliary processes in cases of aphakic glaucoma. Arch Ophthalmol. 1979;97:2135-2138. https://doi.org/10.1001/archopht.1979.01020020453008
11. Roberto GC. Cyclophotocoagulation. In: Ophthalmic surgery: Principles and practice e-book. In: Spaeth GL, Danesh-Meyer H, Goldberg I, Kampik A, editors. Elsevier Health Sciences; 2012. pp. 318–325.

12. Bernard JA, Haut J, Demailly PH, et al. Coagulation de proces ciliares au laser a l'argon. Son utilisation dans certaines hypertonies. Arch Ophtalmol Rev Gen Ophtalmol. 1974;34:577–580.
13. Masters JS, Siegel MJ, Patel AS, et al. Endoscopic Cyclophotocoagulation (ECP). American Academy of Ophthalmology, Eyewiki. August 2021. Available from: https://eyewiki.aao.org/Endoscopic_Cyclophotocoagulation_(ECP). Accessed December 2021.
14. Aptel F, Denis P, Rouland JF, et al. Multicenter clinical trial of high-intensity focused ultrasound treatment in glaucoma patients without previous filtering surgery. Acta Ophthalmol. 2016; 94:e268–e277. https://doi.org/10.1111/aos.12913
15. Giannaccare, G, Vagge A, Sebastiani S, et al. Ultrasound Cyclo-Plasty in Patients with Glaucoma: 1-Year Results from a Multicentre Prospective Study. Ophthalmic Res. 2018:1–6. https://doi.org/10.1159/000487953
16. 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(1):24–30. https://doi.org/10.1097/ijg.0000000000001400