Commentary: High-intensity focused ultrasound - A panacea in the making?

The raised intraocular pressure (IOP) in glaucoma is caused by outflow obstruction and its treatment is aimed at reducing aqueous production (medically or cyclodestruction) or creating alternate drainage pathways (filtering surgery). Cyclodestructive procedures refer to the destruction of the ciliary body and have been traditionally reserved for refractory glaucoma with poor visual potential. This is due to unpredictable and non-selective tissue destruction with a risk of vision-threatening complications related to severe inflammation and hypotony. Currently, the most common cyclodestructive procedures use laser, having superseded cryotherapy, and cyclodiathermy. Efforts to increase the precision of cycloablation to minimize damage to subjacent tissue have led to the development of micropulse diode transscleral cyclophotocoagulation (MP-TSCPC), endoscopic cyclophotocoagulation (ECP), and high-intensity focused ultrasound (HIFU) cyclodestruction. Both MP-TSCPC and ECP use lasers, and ECP is an invasive procedure. In TSCPC, laser energy applied over the sclera is absorbed by the melanin in the ciliary processes, causing coagulative necrosis of the ciliary body and IOP reduction is usually noted at 4–6 weeks post-procedure.[1]

High-intensity focused ultrasound leads to thermic necrosis (80°C) and loss of the ciliary body epithelium at the intermediate and distal portions of the pars plicata, without damage to the blood–aqueous barrier, as seen in ultrastructural studies.[2] This is the reason for the rapid decrease in IOP following HIFU, with the possibility of a slight increase seen in the long-term, due to re-epithelialization. Most treated areas undergo cystic involution. Long-term results have demonstrated a 55% success rate at 3 years, with a facility of repeat treatments.[3] Also, the treated areas are well delineated from the non-treated areas. The other mechanism of IOP reduction with HIFU is the increase in the uveoscleral outflow due to thermic-induced scleral fiber delamination, seen as intrascleral hyporeflective spaces and overlying conjunctival microcysts on anterior segment optical coherence tomography (OCT) and *in vivo* confocal microscopy in the treated areas.[4] The device that offers HIFU is EyeOP1 (Eye TechCare, Rillieux-la-Pape, France) and uses a circular probe with six cylindrical piezoceramic transducers (three superior and three inferior) and comes in three sizes (11, 12, and 13 mm), to plan according to the size of the eye for correct focusing of the ultrasound beam. The target zone is highly focused, being 0.1 × 1mm in size. The procedure is automated, and non–operator-dependent with pre-set protocols.[5]

The reported efficacy at 12 months is between 20.1% and 46% for refractory glaucoma and 23.1% and 38% for patients without previous glaucoma surgery.[5] It is to be noted that studies with higher baseline IOP would report a greater reduction in IOP. Rouland *et al*.[3] reported a 33% overall reduction and a 43% IOP reduction in their success patients at 3-year follow-up; 75% of the patients had received a single treatment. Up to three re-treatments have been reported with HIFU.[3,5] A similar IOP reduction of ~33% at 12 months in ~78% of patients was reported by the only Indian study before this one.[6,7] The current study reports a greater IOP reduction (36.66%) with a higher qualified success at 1 year (89.28%) in Indian eyes.[7]

The major adverse effect of the procedure seems to be related to the ocular surface (conjunctival hyperemia, superficial punctate keratitis, corneal epithelial defects [rare], subconjunctival hemorrhage, and scleral marks) and anterior segment (inflammation, mydriasis, pupil peaking, and cataract progression), mostly treatable without sequelae.[1-7] Hypotony reported with the procedure is mostly transient, with persistent hypotony being remarkably rare.[3,5,6] Macular edema is reported as a rare occurrence in conjunction with continued prostaglandin use.[3] Phthisis bulbi, suprachoroidal hemorrhage, and retinal detachment have not been reported so far. Most of the visual acuity loss reported in the studies done so far is related to disease progression (in failed response) or causes that are not necessarily directly attributable to the procedure.[3,5,6] In summary, the procedure appears to be fairly safe in comparison to other cyclodestructive procedures/filtering surgery. This makes it feasible for use in eyes with useful vision though more studies will be needed to confirm its safety.

High-intensity focused ultrasound, as a treatment of glaucoma, holds great promise. Medical management of glaucoma is dependent on patient compliance and is limited by the extent of IOP reduction. Surgical management is invasive and unpredictable in outcome/complications. It also requires long training to acquire proficiency. Laser-based cyclodestructive procedures risk vision loss or are invasive. High-intensity focused ultrasound being a one-time, non-invasive, automated procedure with transient/treatable adverse reactions will likely make it an attractive option in the near future. If appropriately developed, there may also be a possibility of dose–response titration, related to the extent of ablation. However, there are very few studies, and no randomized controlled trials comparing it with other treatment options (filtering surgery/other cyclodestructive procedures).[1-7] Hopefully, more studies, such as the current one, will provide us with valuable data on safety and efficacy.[7] And hopefully, glaucoma specialists will find a panacea for all glaucoma!

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