Advancements in Glaucoma Treatment: A Review of Novel Therapeutic Options

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Introduction Glaucoma affects over 80 million people globally, posing a significant public health concern.[1] Glaucoma is the leading cause of irreversible visual loss worldwide, with global estimates of glaucoma afflicting up to 111.8 million by 2040[2] . Glaucoma is an optic neuropathy, often characterised by elevated intraocular pressure (IOP), leading to progressive death of the retinal ganglion cells (RGCs)[3] . Studies on the compliance rate of patients to anti-glaucoma eyedrops have shown that up to 80 % of patients fail to adhere to their prescribed glaucoma treatment regimen [4]. The bioavailability of eyedrops has been estimated to be 5 %, making this traditional, age old drug delivery system largely wasteful and inefficient[5] .

Methodology
This review selects treatment advancements from 2018 to 2025 based on:

1. FDA approval or late-stage clinical trials.
2. Mechanisms targeting IOP reduction and RGC preservation.
3. Comparative efficacy over conventional treatments.
4. Availability of quantitative data for outcome analysis.

Results

1. **iDose TR (Travoprost Implant)**
   The iDose TR is a trabecular meshwork implant containing 75 µg of preservative-free travoprost that was first approved by the FDA in December 2023 for the intracameral use in the treatment of POAG and OHT. This is a biodegradable, intracameral implant delivering travoprost over 12 months. This preservative-free travoprost is approximately 25,000 times more concentrated than the travoprost in the 0.004 % ophthalmic eyedrop formulation [6]. Mean IOP reduction from baseline over the 6 time points ranged from 6.6 to 8.4 mmHg for the FE implant group, from 6.6 to 8.5 mmHg for the SE implant group, and from 6.5 to 7.7 mmHg for the timolol group. [7].
2. **HERCULES Negative Pressure Pump**
   The HERCULES negative pressure pump is a wearable, external device approved by the FDA in June 2024, designed for patients with normal-tension glaucoma. It works by applying a mild vacuum around the eye, which reduces ocular surface pressure and consequently lowers IOP. In a clinical study involving 186 patients, the device led to a 100% rate of IOP reduction, with 97% of subjects experiencing a drop of more than 20%. The average IOP dropped from 20.2 mmHg to 12.2 mmHg—a 39% decrease. The treatment was well-tolerated, with eyelid puffiness reported in only 17% of cases [8].
3. **MIGS (Minimally Invasive Glaucoma Surgery**
   Minimally invasive glaucoma surgery (MIGS) has gained traction due to its efficacy and safety profile. Among the most studied new devices are the Hydrus Microstent and Xen Gel Stent. MIGS as the preferred primary surgical intervention, particularly in mild to moderate cases of POAG and NTG associated with cataracts. MIGS, when combined with cataract surgery, provides excellent IOP-lowering effects [9] . Among the different types of MIGS, microhook surgery was the most preferred option [10] . The HORIZON study involving 556 patients demonstrated that 77% of patients implanted with the Hydrus Microstent were medication-free two years after surgery, while Xen Gel Stent users experienced a 30–40% reduction in IOP. Complications were relatively minor, with 10–15% experiencing transient inflammation or hypotony [11] .
4. **DSLT (Digital Selective Laser Trabeculoplasty)**
   This presents an advancement over traditional SLT through its AI-guided, non-contact laser delivery method. The Belkin Vision trial conducted in 2022 on 350 patients reported an average IOP reduction of

5.2 mmHg. The absence of direct ocular contact reduced the incidence of corneal injury and post-operative inflammation, making DSLT a promising alternative for early-stage glaucoma [12]. In a study, 54 patients affected by POAG (76) or PACG (28) undergoing DSLT were enrolled, for a total of 104 eyes. At 1 month follow-up, both the eyes affected by POAG and those affected by PACG showed significantly ($p<0.01$) lower mean intraocular pressure (IOP) (−3.67±2.95 mm Hg and −3.93±2.36 mm Hg, respectively) and lower mean number of IOP-lowering topical drugs taken (−0.62±0.57 and −0.78±0.64, respectively) after DSLT. These reductions remained significant until the 1 year follow-up, both for IOP (−3.76±2.84 mm Hg and 3.67±2.46 mm Hg, respectively) and for drugs assumed (−0.79±0.53 and 0.96±0.47, respectively)[13].

5. **Gene Therapy (MMP-3 Inhibition)**
   Gene therapy targeting MMP-3 offers a promising strategy to enhance aqueous outflow and lower IOP by modifying the extracellular matrix of the trabecular meshwork. In a recent study using recombinant adeno-associated virus serotype 2 (rAAV2) to deliver the human MMP-3 gene, non-human primates demonstrated enhanced MMP-3 activity and improved outflow facility. The gene-treated eyes maintained a significant IOP reduction for up to five months without adverse effects. This approach may also contribute to retinal ganglion cell preservation, positioning it as a potential disease-modifying therapy [14].

Discussion

These novel therapies address key limitations of traditional glaucoma treatment. The iDose TR eliminates the need for daily drops, enhancing adherence. The HERCULES pump introduces a non-invasive, wearable modality suitable for patients with normal-tension glaucoma. MIGS offers long-term control with less trauma than traditional surgeries. DSLT replaces SLT with safer, AI-guided precision. Gene therapy introduces a potential disease-modifying approach by preserving RGCs.

These interventions, supported by robust clinical trials, suggest a shift toward multimodal, personalized glaucoma care. Optometrists can play a pivotal role in early detection, patient education, and monitoring outcomes of these novel therapies.

Conclusion

The integration of sustained drug delivery, AI-assisted laser systems, minimally invasive devices, and gene-based therapies signifies a transformative phase in glaucoma care. These options not only enhance efficacy but also reduce the treatment burden on patients. As primary eye care providers, optometrists must remain informed of these advancements to guide clinical decisions, improve patient outcomes, and participate in multidisciplinary glaucoma management.

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