

Visionary medicine

The future of glaucoma treatments

Introduction

In previous whitepapers and blogs, we have discussed the case for more effective targeting and screening for glaucoma, the leading global cause of irreversible blindness. Knowing who to screen and how to reach them, of course, is only the beginning.

In this paper, we will examine the past, present and future of glaucoma treatments. We will demonstrate how conventional treatments, both surgical and medicine-based, tackle existing challenges, as well as examine the limitations they face.

This paper will also analyse emerging treatments such as stem cell therapy, Rho kinase inhibitors and neuroprotection, along with any barriers these methods face to becoming more commonplace.

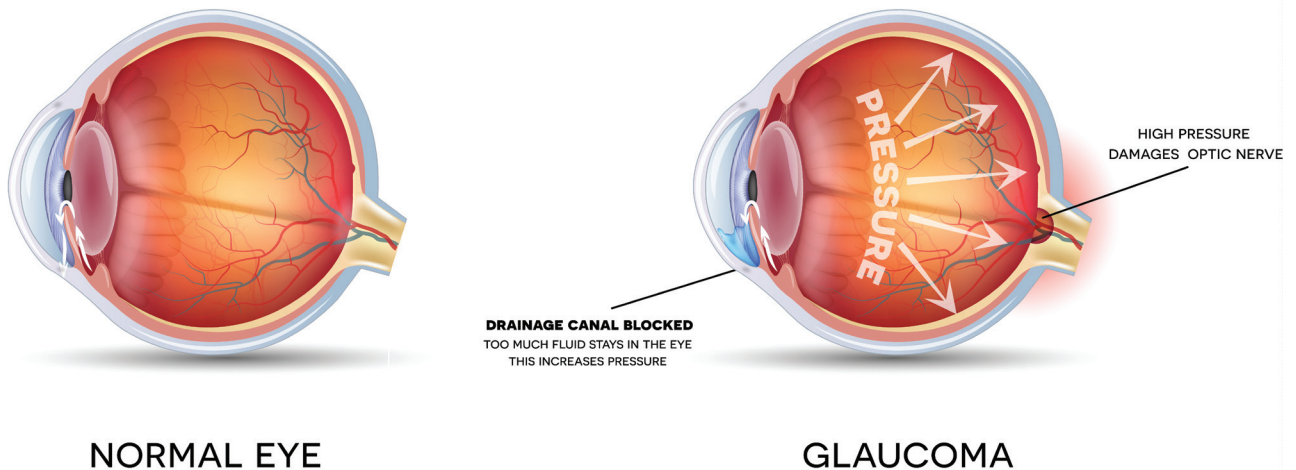
We will also discuss the role of ongoing monitoring of the condition's progression. By keeping and sharing anonymous, digitised records, eye health professionals can contribute to an ongoing global database, building on the good work already done by those identifying groups at high risk of developing glaucoma.

Throughout the paper, in-depth consideration will be given to the patient experience of different methods. By analysing the pros and cons of different treatments, not only from a scientific perspective but also a functional one, methods to boost patient engagement from initial screening to ongoing treatment can be identified.

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Glaucoma: A recap



In the simplest terms, glaucoma is a condition which combines structural changes in the eye's optic nerve head with loss of sight over an extended time period.

In the majority of cases this is due to rising pressure within the eye, referred to as intraocular pressure (IOP). Here, the aqueous humour in the eyeball is unable to drain, damaging both the optic nerve and the retina's nerve fibres.

However, roughly 30% of diagnosed cases of primary open-angle glaucoma (POAG), the most common form of glaucoma, do not involve this pressure build-up, meaning that while raised IOP most often accompanies glaucoma, it does not form part of the condition's definition.

Where there are changes to the structure of the eye without loss of vision, or indeed vice versa, patients are defined as a suspected case, but may be treated in the same way as a confirmed case.

Detecting glaucoma involves several short tests, ideally administered during the same appointment to ensure consistency. These include:

- **Tonometry**, where intraocular pressure is measured using a tonometer.
- **Gonioscopy**, where the eye's drainage canal is examined between the cornea and the iris to check whether it is open (and functioning) or blocked.
- **Visual field tests**, in which one's peripheral vision is checked to identify missing areas of vision, an early sign of glaucoma.
- **Visual acuity tests**, where one's sight is measured at various distances, similar to a visual field test.

- **Pachymetry**, in which the thickness of the cornea is measured using a pachymeter, which produces an echogram of the cornea to gauge IOP.

- **Dilated eye exams**, where the pupils are dilated with eye drops to allow the retina and optic nerve to be examined for changes in the shape and colour of the optic nerve fibres.

What these methods have in common is the fact that, generally speaking, they are capable of detecting the POAG at the pre-symptomatic stage as the symptoms of glaucoma aren't picked up by an individual until relatively late in the condition's development when it reaches the centre of the eye.

With this in mind, the importance of early and regular testing cannot be overstated, especially if one falls into the most at-risk groups. These groups are:

- black people aged over 40
- anyone aged over 60
- those with a family history of glaucoma.

Existing glaucoma treatments

Just as critical as detecting glaucoma early is facilitating quick access to treatment, as loss of sight brought about by the condition is irreversible.

Treatment can involve medication, either on its own or in conjunction with surgical procedures. The Glaucoma Research Foundation identifies five therapeutic medications, classified by the active ingredients they contain:

- **Prostaglandin analogs** work by boosting the eye's ability to drain aqueous humour, reducing intraocular pressure by between 25 and 30%. Xalatan, Lumigan, and Travatan Z are three examples of branded prostaglandin analogs.



- **Beta blockers**, by contrast, decrease the rate at which the eye produces aqueous humour. Widely available in generic formulations, they tend to be inexpensive. Timolol is a beta blocker commonly used to treat glaucoma.
- **Alpha agonists** like Alphagan P and Iopidine perform both tasks, decreasing the rate at which the eye produces fluid and boosting the outflow facility. It also breaks down into the natural composition of tears, making it less likely to irritate the eye.
- **Carbonic anhydrase inhibitors** (CAIs) come in both eye drop and pill forms. They also lower intraocular pressure by slowing down production of fluid.

Surgical options for treatment involve making adjustments to the eye's drainage capacity, either widening existing channels or creating new ones to augment outflow.

A **laser trabeculoplasty** involves an ophthalmologist using a high-precision laser to open up holes and widen the eye's filtration system. This technique was introduced in 1979 as argon laser trabeculoplasty (ALT), but did not replace medication as a primary treatment for POAG due to attrition to the affected tissue over time.

Advances to this technique have been made in recent years, resulting in a selective laser trabeculoplasty (SLT). Here, the process is largely the same except without any risk of damage to the surrounding tissue, meaning the process can be safely repeated.

A **trabeculectomy**, meanwhile, is a more conventional surgical procedure where an entirely new opening is created

by opening a hole in the eye's drainage system. This method is 60-80% effective when it comes to lowering intraocular pressure and is generally employed only when medication and laser surgery fail to secure an improvement in early cases of POAG. In advanced cases, however, it is recommended as a first-line approach.

Side effects of existing glaucoma treatments

None of these treatments are perfect, some carry the risk of side-effects, which must be weighed against the vision loss caused by the glaucoma itself.

With eye drop medication, as with any ongoing programme of medication, it's up to the patient to remember to administer it. The reality of daily life means that this doesn't always happen. Likewise, the cost of long-term medication can prove prohibitive for patients in some countries.

There are also possible side-effects specific to each active ingredient:

- Prostaglandin Analogs: Possible changes in eye colour and eyelid skin, blurred vision, eye redness and irritation.
- Beta Blockers: Low blood pressure, reduced pulse rate, fatigue, shortness of breath, reduced libido, depression.
- Alpha Agonists: Eye irritation, fatigue, headache, drowsiness, dry mouth or nose, increased possibility of an allergic reaction.
- Carbonic Anhydrase Inhibitors: Eye irritation in eye drop form. Tingling hands and feet, stomach upset, memory problems, depression, frequent urination in pill form.

With surgical methods, side-effects and other considerations also present themselves. In the case of a laser trabeculoplasty, even if successful, the results are typically not permanent and require ongoing medication (usually eye drops, themselves carrying the above risk of side-effects). This surgery also brings a slight increase in the risk of cataracts and unless a selective laser trabeculoplasty is performed, the procedure cannot be carried out more than once.

A trabeculectomy is generally limited to two surgeries per eye, can leave scarring and carries a risk of conjunctival leak. There is also, as with any traditional surgery, a small risk of infection, as well as the possibility of hyphaema, although this usually settles very quickly.



Pioneering treatments for glaucoma

As things stand, the objective of current glaucoma treatments is to lower IOP to the point where the rate of visual loss is unlikely to impact a patient's quality of life during a reasonable time period; that of their lifetime.

The future of glaucoma treatment, then, lies in finding new ways to keep the eye's drainage system, the trabecular meshwork, clear without intrusively irritating or damaging the surrounding eye. Ultimately, the goal is a reversal of sight loss caused by glaucoma.

Some emerging treatments will focus on improving the existing goal of long-term symptom management, while some will push towards reversal.

Rho kinase (ROCK) inhibitors are an emerging category of medication which work by reducing the stiffness of the cells in the trabecular meshwork, allowing easier and more natural drainage from the eye. This contrasts with existing medications which simply reduce production of aqueous humour or push for more drainage without improving the 'quality' of the tissue itself.

Rock inhibitors are currently in early-phase R&D, with promising research data showing potential for neuroprotective and anti-inflammatory effects as well as those mentioned above.

Stem cell therapy is a field which shows huge promise in many medical applications, and glaucoma is no different. Not only have studies shown potential for protecting the optic nerve from further damage, these treatments might also replace degenerated tissue within the trabecular meshwork and optic nerve itself.

This is incredibly exciting, but in order for this to become a reliable therapy, it's necessary to fulfil several criteria.

Not only must stem cells be implanted safely into specific locations within the eye, they must connect properly with specific parts of the brain and remain stable for prolonged periods of time. As of yet, these criteria have not all been satisfied. Glaucoma patients should not consider this option (if indeed it is offered to them) without the assurance of a thorough clinical trial setting.

The importance of screening and monitoring

Whether using and refining existing glaucoma treatments or developing a knowledge base necessary to develop new ones, it is vital that eye health professionals do all they can to promote a proactive culture of screening among those groups most at risk.

The benefit of this is two-fold. Obviously, an individual patient benefits from paying close attention to their health, and monitoring can pick up early signs of glaucoma long before symptoms present.

Meanwhile, collecting data on a large and coordinated scale means the ophthalmic community can assess the influence of multiple factors and, ultimately, gain a better understanding of glaucoma.

Guidance from the National Institute for Care and Excellence (NICE) points out that there is currently no available evidence from randomised control trials that might help isolate and help those groups most at risk. Those identified with glaucoma follow a standard pattern of monitoring, alongside a lifetime of treatment.

Growing the body of evidence available to us through monitoring will allow us to pinpoint the rate at which the condition develops when certain factors are in play. In the short term, this allows patients with slower-



progressing glaucoma to avoid having to go to unnecessary appointments, which are needlessly time-consuming for all involved.

In the longer term, this means patients with more aggressive glaucoma can enjoy having more resources allocated to monitoring and treatment. Given the fact that, in many countries, the demographic groups most at risk of developing the condition are those with the most limited access to eye health clinics, those resources can also be spread around to promoting more effective and regular screening in the community.

More data also means a better grasp of what signs to look for, and the factors exacerbating those signs. Using advanced tools like the Henson Perimeter, informed ophthalmologists can test with an unprecedented level of specificity.

This might involve repeating tests to ensure no signs are missed or testing around missed locations with additional stimuli. For patients needing to monitor an ongoing case of glaucoma, this ensures nothing is missed when it comes to charting its progression.

"The discovery of effective ways to ensure the early diagnosis of glaucoma is essential."

"The Henson 9000 screening programs are quick and precise, providing eyecare professionals with a reliable tool for understanding the prophylaxis of the condition. The programs are user-friendly and not only save time but are highly suitable for examining large groups of at-risk patients."

- Polly Todorova



Henson 9000 Perimeter



In conclusion

With a condition like glaucoma, whose treatment promises to push the expanding frontier of medical science but still, paradoxically, remains largely unchanged for some time, we need to look at the entire process. From diagnosis to treatment, if any details can be brought to light, it needs to be done through a rigorous process of data collection and analysis on a global scale.

This leads to a better informed medical community worldwide, and patients with a more in-depth perspective of their treatment. Often a patient will google their own condition and find themselves unsatisfied with their own treatment, having misinterpreted certain statistics or taken them out of context. Better access to relevant stats will help build trust between patients and the ophthalmic community.

All of this needs to happen sooner rather than later. The reality of a growing and aging global population means that the future of dealing with glaucoma will come sooner than many hope for.

To support the development of ground-breaking new treatments, effective screening and monitoring will allow ophthalmologists on the front lines of the fight against glaucoma to make a huge, lasting contribution.

