

Management of the Progressing Glaucoma Patient

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Abstract

The objective of glaucoma therapy is to preserve the patient's vision at moderate cost. Life expectancy, stage of disease and progression rate, jointly, are considered the pivotal standard of assessment of the glaucoma patient, and correct therapeutic management is fundamental. Decreasing the progression rate of functional damage is the only strategy to reach the therapy objective in glaucoma today. From this point of view, ocular hypotensive therapy represents the only available instrument to reduce the risk of progression, minimising the risk of visual loss for each patient. Decreasing intraocular pressure should be considered the instrument by which the clinician can reduce the speed of a patient's disease progression. The choice of aggressive or less aggressive treatment can be made on a case-by-case basis to slow down the progression rate of the disease to a secure level for the patient's individual risk profile. In conclusion, the management of the glaucoma patient should be based on perimetric data, which should be considered as the way to judge the efficacy of the ocular hypotensive therapy.

Keywords

Glaucoma, ocular hypotensive therapy, prostaglandin analogues, progression rate

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The objective of glaucoma therapy is to preserve the patient's vision at moderate cost.¹ It is a common perception that glaucoma has a slowly progressing pathology and that the visual function of the patient suffering from glaucoma deteriorates symptomatically only towards the terminal stage of the disease. In fact, scientific proof exists demonstrating how progression rate can be very variable from patient to patient.² At an unexpectedly early stage of the disease the glaucoma patient can experience such a loss of vision that his or her quality of life changes. This is reflected in an increase in accidental slips and falls³ and road accidents⁴ observed in elderly glaucoma patients compared with persons of the same age without glaucoma. Currently, the correct clinical management and therapeutic approach for the newly diagnosed patient cannot disregard an initial assessment of the individual's lifetime risk of developing perimetric damage that will compromise quality of life.

Risk assessment is based on some fundamental elements, among which stage of pathology at the moment of diagnosis and age of the patient (and his/her life expectancy) play a primary role. The younger the patient presenting with advanced glaucoma at first diagnosis, the bigger the risk that progression of the disease will lead to serious visual impairment. By contrast, advanced age and the presence of damage at an initial stage can be considered, under this point of view, to be elements of a low risk profile.

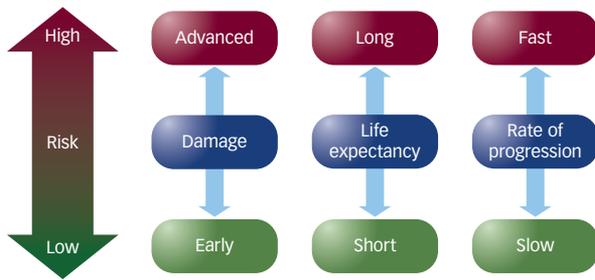
The third and most important factor to be considered, next to age and damage stage, is the progression rate of the disease during a patient's

life (see *Figure 1*). The risk of developing serious visual impairment, starting with the same age and same stage of functional damage, increases with the acceleration of disease progression. In other words, a young patient with an advanced stage of the disease but with slow progression has an overall lower risk of visual impairment than a patient of the same age and similar disease stage whose disease progression is very rapid (see *Figure 2*).

Life expectancy, stage of disease and progression rate are considered the pivotal standard of assessment of the glaucoma patient. This assessment is fundamental in ensuring correct therapeutic management of the condition. Preserving a patient's visual function is the objective of glaucoma therapy. However, decreasing the progression rate of functional damage is the only strategy by which to reach such an objective today. From this point of view, ocular hypotensive therapy represents the only available instrument by which to reduce the risk of progression,⁵⁻⁹ minimising the risk of visual loss for each patient. The novelty, in terms of concept, is to consider the decrease of progression in functional damage as a measure of efficacy for the ocular hypotensive therapy, rather than relying on the associated value resulting from the tonometric value.

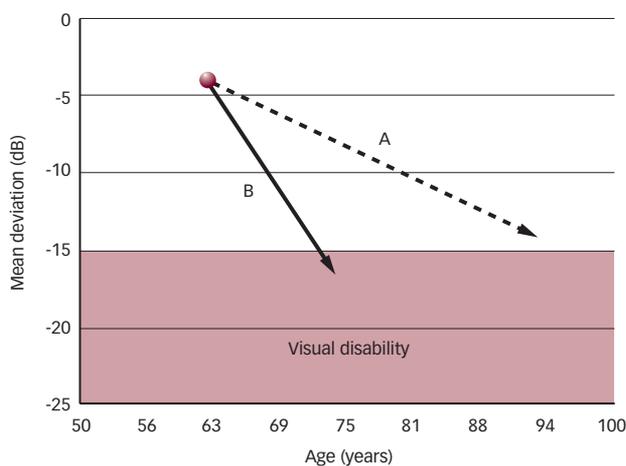
Intraocular pressure (IOP) should therefore be considered the instrument by which a clinician can judge the speed of progression of a patient's disease. The choice of aggressive or less aggressive treatment can be made on a case-by-case basis in order to slow down the progression rate of the disease to a secure level for the patient's

Figure 1: Factors Affecting the Individual Risk of Visual Disability



The individual risk of developing symptomatic functional glaucoma damage depends on the relationship between the stage of the damage, life expectancy and the progression rate of the disease.

Figure 2: Age/Function Diagram

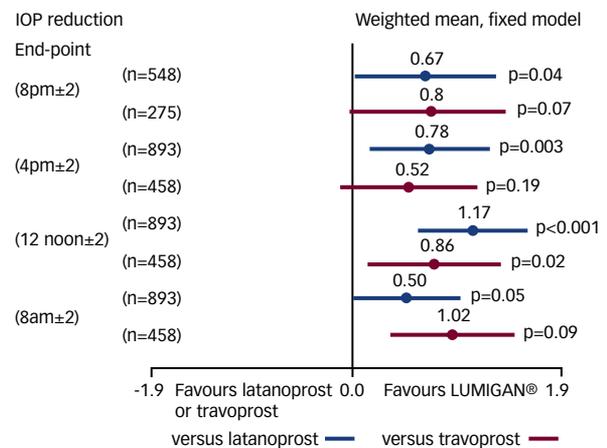


Patients with the same age and same initial stage of functional damage. Patient B has a higher risk of reaching visual disability, as his disease is progressing more quickly than that of patient A.

individual risk profile. Thanks to the availability of new statistical software aids integrated into the most commonly available visual field analysers, today it is possible in clinical practice to estimate the progression rate of functional measures (e.g. mean deviation or visual field index) from series of visual fields taken over time,¹⁰ allowing changes in the progression rate to be assessed at different stages of the disease or before and after therapeutic interventions, whether medical, laser or surgical. Such software allows clinicians to assess variation in glaucoma development rate following therapeutic intervention, either medical, laser or surgical. For a patient with a documented clinical and functional history it can be relatively easy to measure glaucoma progression rate before and after the therapeutic intervention to assess its efficacy. A new patient without a history that can characterise the pathology before the diagnosis is a separate matter. Without historical functional data, the estimation of an individual's risk should be based on the stage of damage at the point of diagnosis, the patient's life expectancy and an assessment of the risk of progression based on the presence of known factors. These factors include a higher IOP at diagnosis, presence of pseudoexfoliative material or pigmentary dispersion in the anterior segment.

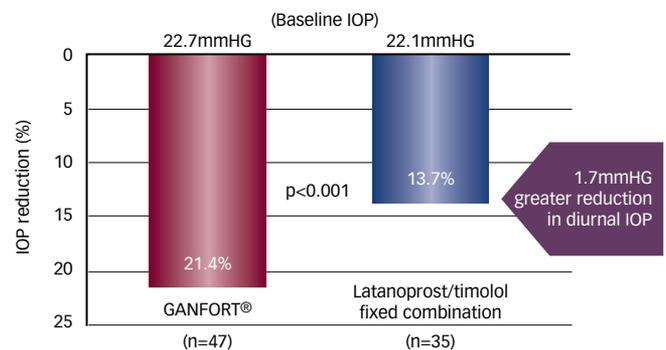
Information referring to life expectancy, stage of damage and estimation of the probable progression rate is integrated in order to guide the grade of therapeutic intervention needed in the newly diagnosed patient. This information aids the choice of the

Figure 3: Difference in Mean Reductions from Baseline Intraocular Pressure versus Latanoprost and Travoprost



Adapted from Aptel et al., 2008.¹³

Figure 4: Mean Intraocular Pressure Reduction (%) from Baseline at Three Months



Adapted from Centofanti et al., 2009.¹⁴

most appropriate treatment, whether monotherapy, combination therapy or parasurgical/surgical therapy. In the case of a patient with a middle/low-risk profile, the choice is usually a monotherapy of proven ocular hypotensive efficacy. Scientific literature on one side and clinical practice on the other have confirmed that among the drugs available today, the prostaglandin analogues and the prostamides are probably the classes with the highest ocular hypotensive efficacy.^{11,12}

A recent meta-analysis published in the *Journal of Glaucoma*¹³ has shown that among the drug classes mentioned above, the prostamide analogue bimatoprost has the highest ocular hypotensive efficacy (see Figure 3).¹⁴ The difference in ocular hypotensive efficacy between bimatoprost and the other prostaglandin analogues could be considered small from a clinical point of view (about 1mmHg). However, it may have relevant consequences for the prognosis of long-term visual function of the glaucoma patient under ocular hypotensive treatment.

The Early Manifest Glaucoma Trial (EMGT) clearly demonstrated that every additional decrease of 1mmHg IOP compared with baseline obtained with therapy reduces the risk of disease progression by 13%.⁵ In addition, the EMGT showed that IOP reduction obtained during the first three months of therapy is significantly linked to a reduction in risk of disease progression (-11%). This underlines how early therapeutic intervention, in addition to its efficacy, plays a fundamental role in the prognosis of long-term visual function.

The strong link between the amount of IOP reduction and drop in disease progression risk has recently been confirmed by the Canadian Glaucoma Study (CGS). The CGS was a multicentre, prospective, longitudinal clinical study that started with the aim of identifying ocular and systemic risk factors for the progression of perimetric damage in glaucoma.⁶ In the CGS, risk factors of a cardiovascular nature, such as peripheral vasospasm, migraine or systolic and diastolic blood pressure, did not appear to be significantly associated with the progression risk of glaucomatous damage. However, every 1mmHg increase in IOP has been associated with an approximately 20% increased risk of progression.

What stands out from the trial data is that therapeutic management of the glaucoma patient needs to be early and that effective prevention of increased IOP is essential, since long-term prognosis is linked to the effectiveness of therapy started at the moment of diagnosis.

If the management of patients with a middle/low-risk profile consists of choosing an effective monotherapy, the approach is different for patients with higher-risk profiles. Those with high-risk profiles include young patients with advanced damage and a fast progressing disease or those with a high probability of rapid disease progression who could require more aggressive therapies from the time of diagnosis or very early during follow-up.

The probability that two years after diagnosis a glaucoma patient needs more than one drug to decrease his or her IOP to an acceptable value based on individual risk profile has been estimated to be 75%.⁷ If it is necessary to combine more drugs to lower IOP, not only efficacy but also efficiency must be considered. To be efficient from a clinical point of view, a therapy must not only be effective on IOP, but must also have a good local and systemic tolerability. It must require few daily applications to aid the patient's compliance during periods between visits.

From this point of view the fixed combinations with beta-blockers and prostaglandin derivatives constitute an important tool. These combinations are effective in lowering IOP and have an excellent tolerability, and daily posology is reduced to a minimum. Recently, some studies have been published reporting the assessment of combinations of beta-blockers and prostaglandin analogues in patients previously treated with monotherapies. In the study published by Martinez et al. in 2008, the efficacy of the fixed combination

therapies of bimatoprost or latanoprost with timolol have been compared in a patient population previously taking beta-blocker monotherapy.¹⁵ The results showed that both fixed combination therapies were superior to monotherapy with beta-blockers in reducing IOP. The combination with bimatoprost was superior to the one with latanoprost. These results confirm data from the literature comparing prostaglandin analogues administered in monotherapy.¹³ These data also agree with the results of a randomised multicentre study where the efficacy of fixed combination therapies has been compared in a population of glaucoma patients previously treated with prostaglandin analogue monotherapy (see *Figure 4*).¹⁶ Although the decrease of IOP is today the only evidence-based instrument capable of altering the visual function prognosis of the patient suffering from glaucoma, it should be considered that the ultimate goal of therapeutic intervention is not IOP reduction. The goal is deceleration of disease progression rate to a level that minimises the impact of the functional deficit on the quality of life of each individual patient.

Conclusion

In conclusion, management of the glaucoma patient should be based on perimetric data, which should be considered as the best way to judge the efficacy of ocular hypotensive therapy. This should allow a more solid relationship to be built between the physician and the patient based on mutual exchange of information. The clinician will gain information regarding the variation in disease progression rate in response to the therapeutic choice, with evident functional prognostic implications. On the patient's side, there is the potential to discuss compliance and the perception of the disease during follow-up. ■

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