

## Intraocular Pressure: Protagonist or Supporting Actor in Glaucoma?

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### ABSTRACT

Glaucoma, one of the principal causes of visual disability and blindness around the world, is considered a progressive form of optical neuropathy often associated with elevated intraocular pressure (IOP) consequent on abnormal elevated resistance to draining of aqueous humour (AH) through the trabecula (TM) and the Schlemm's canal. Despite in-depth researches, its aetiology still remains to be clarified. However, all authors agree that the main risk factor on which it is possible to act therapeutically is elevated intraocular pressure (IOP).

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**Key words:** Glaucoma; IOP; Optical neuropathy; Aqueous humour

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### REVIEW

Glaucoma, one of the principal causes of visual disability and

blindness around the world, is considered a progressive form of optical neuropathy often associated with elevated intraocular pressure (IOP) consequent on abnormal elevated resistance to draining of aqueous humour (AH) through the trabecula (TM) and the Schlemm's canal. Despite in-depth researches, its aetiology still remains to be clarified. However, all authors agree that the main risk factor on which it is possible to act therapeutically is elevated intraocular pressure (IOP).

Actually, a vast range of clinical studies on a wide scale is in agreement that the objective of therapy must be to maintain an IOP level such as to arrest the progression of the glaucomatous process<sup>[1,2]</sup> keeping repercussions on patients' quality of life to the minimum. In this connection, reduction of IOP, especially if carried out in an early phase of the illness, not only reduces or arrests its evolution, but can involve improvement of psychophysical visual sensitivity, with an increase in amplexness of PERG<sup>[3]</sup> and in any case a reduction in the typical progressive loss of the visual field<sup>[4]</sup>.

It has been found that alongside glaucoma patients with raised IOP (HTG) there are others in whom determination of IOP with the traditional methods shows it to be within the normalcy range (glaucoma with normal pressure, NTG) and this observation has challenged the real role of IOP. Fluctuations in IOP and their entities are therefore considered most relevant.

Study of variation in intraocular pressure with tonometric curves<sup>[5]</sup> has shown that it presents a typical sinusoidal pattern with the acrophase in the nocturnal hours, probably because of the lying position taken up by the subject during sleep. During the day too fluctuations are quite frequent, with differences in values above 6 mm of Hg. This involves a further risk for the optic nerve<sup>[6,7]</sup>, and hence the need for a diurnal and possibly nocturnal tonometric check, which is possible today through devices like contact lens sensors<sup>[8]</sup>.

Fluctuations are numerous and larger in subjects with type A personality<sup>[9,10]</sup> in whom progression of the damage to the visual field proves to be accelerated. The increase in IOP in these patients could also be connected to the action of catecholamines on the beta-2 receptors situated in the pigmented epithelium of the ciliary bodies, which, as is well known, involves an increase in synthesis of cyclic

AMP (AMPC) with a consequent increase in the production of aqueous humour, one of the factors on which intraocular pressure depends.

IOP is the result of the balance between the quantity of aqueous humour that the eye produces and the facility with which it leaves the eye, according to Goldmann's classical equation:  $P_o = (F/C) + P_v$ . [ $P_o$  = IOP in millimetres of mercury (mm Hg), F = velocity of aqueous formation, C = facility of outflow and  $P_v$  = episcleral venous pressure].

Fluctuations in and imperfect control of IOP may also depend on poor compliance of the patient due to the chronic nature of the treatment and the side effects that the therapy involves. In this connection, it has been observed that using preparations devoid of BAC (Benzalkonium chloride) the compliance markedly increases, and the quality of life, evaluated with the OSDI questionnaire (Ocular Surface Disease Index), is clearly improved<sup>[11]</sup>.

The pathogenetic role of IOP fluctuations imposes the use of medicines with long-term action. Indeed, it is only in this way that the range of diurnal fluctuations can be reduced<sup>[12]</sup> with deceleration of the glaucomatous damage. A more marked reduction in fluctuations can be obtained by means of trabeculectomy. As K. Mansouri *et al* observe<sup>[13]</sup> this procedure determines a statistically significant increase in reduction of the average values of the diurnal tonometric curve, also reducing the size of the fluctuations in comparison to what is observed in subjects in pharmacological treatment (Latanoprost). This study highlights the pathogenetic role in regulation of IOP played by the trabecula, whose endothelial cells, organized in a three-dimensional network, interact with the free radicals that are formed in the aqueous humour.

Morphological and biochemical analyses of the trabecula of patients with POAG have revealed loss of cells, greater accumulation of proteins of the extracellular matrix (ECM), changes in the cytoskeleton and cellular ageing<sup>[14]</sup>. Hence the trabecula constitutes the fabric target of glaucoma and its development and progression accompany oxidising damage to it, as is confirmed by various studies<sup>[15,16]</sup>, which have also stressed that the medicines used for IOP reduction are substances with antioxidant activities able to protect the cells of the trabecula and their mitochondrial components.

Damage to the trabecula could point to a genetic predisposition<sup>[17]</sup>, shown to be frequent in blood relations of subjects with POAG, as the basis on which oxidizing stress would act, in turn triggering, with further cellular damage, the increase in IOP.

This increase is responsible both for the damage to the ganglionic cells, with activation of apoptosis and consequent irreversible deficits of the visual field, as observed in animal models<sup>[18,19]</sup>, and for the further damage to the cells of the trabecula. A vicious circle would thus be activated that is destined to maintain itself with progressive damage to the ganglionic cells.

Recently, on the basis of observations in experimental animal models, the hypothesis has been put forward that an increase in IOP may also be consequent on a NO (Nitric oxide) deficit. This deficit, as is well known, favours the outflow of aqueous humour from the anterior chamber, reducing the volume of the cells of the trabecula and, through relaxation of the smooth musculature, favouring expansion of the Schlemm's canal. Ultimately, the increase in IOP would be the result of the convergence of various factors that each time can variously overlap.

Hence, from what has so far been acquired, it can be concluded that IOP plays an ambivalent role, behaving as a risk factor in certain respects and as a consequence of the glaucomatous process in others. Thus the relationship between IOP and glaucoma, though evident, in various respects still needs to be clarified.

## CONFLICT OF INTERESTS

The author has no conflicts of interest to declare.

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