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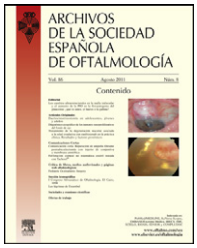

Editorial

Ultrastructural changes in the trabecular meshwork and increased IOP. Which came first, the chicken or the egg?☆,☆☆

Los cambios ultraestructurales en la malla trabecular y el aumento de la PIO en la fisiopatogenia del glaucoma: ¿qué es antes, el huevo o la gallina?

M. Galdos[a,*], *E. Vecino*[b]

[a] *Servicio de Oftalmología, Hospital de Cruces, Instituto Clínico Quirúrgico Oftalmológico (ICQO), Departamento de Biología Celular e Histología, Universidad del País Vasco, Leoia, Bizkaia, Spain*

[b] *Departamento de Biología Celular e Histología, Universidad del País Vasco (UPV/EHU), Leoia, Bizkaia, Spain*

It is known that the trabecular mesh undergoes ultrastructural changes with aging that appear to prevent the collapse of trabecular spaces and Schlemm's canal. The sheath of the elastic fibers thickens together with the connecting fibrils and extracellular material deposits in the cribform region (the outermost trabecular mesh adjacent to Schlemm's canal).[1] It is significant that these changes are morphologically the same as those exhibited by glaucoma patients, with said thickening of sheets and fibril material deposits being quantitatively higher than controls of the same age.[2]

On the other hand, there are mechanic/sensory pathways which demonstrate that mechanical stimuli (such as increased IOP) become an expression of molecules that could induce extracellular matrix expression and drive the above ultrastructural changes at the trabecular mesh.[3]

Recently, while trying to determine which possible ultrastructural changes could induce an increase of IOP in the cribform region, the following study was carried out. By means of episcleral veins cauterization (respecting the trabecular tissue) it was possible to induce sustained IOP increases during 14 months in the left eyes of young and healthy Gottingen minipigs (after documenting the optic disk prior to the glaucomatous changes). After completing the research and obtaining glaucomatous changes in the optic disk, an ultrastructural analysis of the trabecular mesh was carried out with transmission electronic microscopic, comparing the ultrastructure of the right eyes (controls) with the glaucomatous left eyes. It was observed that the glaucomatous eyes exhibited fibrillar material increase in the subendothelial cribform region, preferably at the level of the connecting fibrils and elastic fibers of said region, together with an increase of cellular organelles responsible of protein syntheses (rough endoplasmatic reticulum).[4]

The above findings bring us back to a question already posed by Lütjen-Drecoll et al. in 1986, suggesting that IOP could account for the ultrastructural changes in OAGP, but said authors discarded this possibility on the grounds that these changes do not occur in pseudo-exfoliative glaucoma.[5] It is possible that the pseudo-exfoliative material obstructing the trabecular mesh could interfere in the changes caused by IOP in the trabecular mesh in open angle glaucoma because it interferes differently in mechanic/sensory pathways.

After analyzing in great depth our material and comparing the trabecular mesh of control eyes against those subjected to sustained IOP increase, we can conclude that it is possible that increased IOP may induce an activation of these mechanical-sensory pathways, thus activating and stressing trabecular

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* *Corresponding author.*
E-mail address: marta.gal2@gmail.com (M. Galdos).

mesh cells and increasing the syntheses of extracellular material. Said extracellular material leads to the ultrastructural changes typical of glaucoma in the cribform mesh spaces and Schlemm's canal. However, the progression of these changes inexorably leads to the opposite effect, i.e., the obstruction of the aqueous humor flow in the external region of the trabecular mesh and the onset of a vicious circle that generates IOP increases. It appears that treatment can partially slow down this vicious circle by reducing IOP. However, the progressive nature of glaucoma and the recurring IOP increases are characteristic of this disease and require more drugs. It is likely that the IOP peaks that are not controlled by medical treatment or those generated by the poor compliance of patients could continue to contribute to obstruct the trabecular mesh and therefore increase IOP, thus maintaining the activity of said vicious circle. This would explain the progressive nature of IOP control in glaucoma which generally requires increases in the number of drugs leading up to surgical treatments.

More research is required at this level for a definitive confirmation of these findings and in order to make progress in clarifying the physiopathogeny of glaucoma.

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