Editorial

Evaluation of optic nerve perfusion in optic neuropathies and neurodegenerative diseases

Evaluación de la perfusión del nervio óptico en las neuropatías ópticas y las enfermedades neurodegenerativas

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Research on the etiopathogenesis of some optic neuropathies such as glaucoma has evidenced the importance of the mechanisms involved in the vascular supply and the regulation of blood flow to the optic nerve head (ONH).\textsuperscript{1,2} The utilization of devices measuring vascular flow in the papilla, as well as the assessments of other optic disc characteristics such as color, have provided new opportunities for discerning the factors involved in axonal damage of retina ganglion cells in various pathologies, including neurodegenerative diseases. Likewise, this technology is useful in patients with uncertain diagnostic such as cases exhibiting atypical papillary morphology or inconsistencies between functional and structural tests.

In contrast with other parts of the ocular globe, the ONH receives its vascular supply mainly from 2 systems: the most superficial layers (i.e., the retina nerve fiber layer) which are irrigated by branches of the central retinal artery, while the deeper layers (the lamina cribosa and retrolaminar portion) receive most of its vascularization from the short posterior ciliary arteries. The self-regulation capacity of the blood flow in the optic disc in response to changes in ocular perfusion pressure occurs due to neurovascular coupling in endothelial cells as well as the neuroglya (as in the rest of the retina), as well as to the molecules that are distributed from the choriocapillary (such as nitric oxide or endothelin), due to the close anatomic relationship between the ONH and the choroids.\textsuperscript{3} For instance, multiple sclerosis patients exhibit high levels of endothelin in circulation, which would contribute to a reduction in blood flow to the ONH.\textsuperscript{4}

Numerous methods have been utilized for studying papillary perfusion. Fluorescein angiography (which allows in-depth studies of the most superficial retina vessels) or indocyanine green (utilized for studying the choroidal circulation) are very helpful for diagnosing diseases affecting the retina of the choroids. However, they only allow us to see a few optic disc vessels and do not provide a lot of information as regards perfusion. Doppler laser or speckle laser \textsuperscript{5} flowmeters provide information about the velocity of blood flow in the ONH. The measures provided by both methods are highly variable and dependent on the strength of the signal, and provide information only about a small optic disc area. Quite recently, ultrafast angio-OCT devices have been developed capable of providing 3-D images for studying microcirculation in the ONH. In recent years a number of publications have reported findings with the use of this new technology in patients with optic neuropathies

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such as glaucoma, observing a statistically significant reduction of flow and vascular density in the papilla of subjects with glaucoma when compared to a group of healthy subjects. On the other hand, Wang et al. applied angio-OCT to measure blood flow in the optic disc of patients with multiple sclerosis, identifying a significant reduction of the flow index against the control group, particularly in patients with optic neuritis history.

Accordingly, it is evident that the study of blood flow to the ONH and the self-regulation thereof are key to understand damages affecting the neurons comprising the nerve. Research in animal models such as monkeys reports that this self-regulation capacity of the optic nerve is more vulnerable to ocular perfusion pressure reductions (caused by systemic arterial pressure drops) than to intraocular pressure increases induced by various mechanisms. Similarly, it has been established that the hypoxia and reperfusion events which take place during the night in patients with obstructive sleep disorder enhance the development and progression of optic nerve damage, due to it being more susceptible to intraocular pressure fluctuations or increases.

ONH perfusion depends on 3 factors: blood flow index (discussed above), oxygen saturation and hemoglobin concentration. Utilizing hemoglobin as reference pigment, a group of ophthalmologists, opticians and engineers of La Laguna University have developed a software (Laguna ONhE®) for studying hemoglobin concentration changes in different areas of the optic nerve predetermined by the program on the basis of a color photograph of the papilla. The application of the software in patients with glaucoma has already produced results, obtaining a high balance between sensitivity and specificity together with high reproducibility and strong correlation with other functional and structural tests utilized in the analysis of this neuropathy. The systems for interpreting images (in this case fundusscopic photographs of the papilla) receive the light reflected in different wavelengths (blue, green and red). The areas with high hemoglobin concentration reflect a higher proportion of red light, whereas atrophic areas or poorly vascularized tissue reflect a higher proportion of green and blue which are not absorbed by the blood. The eye perceives this as a paler shade, which had been observed in patients affected by neurodegenerative diseases, particularly multiple sclerosis (Fig. 1). The application of the Laguna ONhE® color identification software with a group of multiple sclerosis patients established the existence of a lower amount of hemoglobin against the group of healthy subjects, above all in the temporal area sectors (which had already been described with conventional ocular fundus observation of these patients).

Therefore, even though direct observation of the papilla through ocular fundus exploration continues to be a necessary and essential method for initial diagnostic evaluation and follow-up of patients with pathologies involving the optic nerve, the digital imaging analysis techniques and the measurement of blood flow or changes in color constitute an important aid for early detection and quantification of damages, in addition to enabling a better understanding of the etiopathogenic processes and facilitating therapeutic action. Likewise, traditional exploration continues to be necessary and obligatory for a neuro-ophthalmological assessment of patients with neurodegenerative diseases. However, technologies for assessing ONH perfusion enable early detection of neurological damage at the ocular level, because optic atrophy is detectable by the human eye only when over 50% of ganglion cell axons has been lost. Said techniques could be a useful tool for improving early detection, differential diagnostic and follow-up of these patients.

**Conflict of interest**

No conflict of interests has been reported by the authors of this paper.

Professor González de la Rosa has a proprietary interest in the Laguna ONhE® software.
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