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REVIEW

Reactive oxygen species, oxidative stress, glaucoma and hyperbaric oxygen therapy

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Glaucomas;
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Abstract This review examines the role of oxidative stress in damage to cells of the trabecular meshwork and associated impaired aqueous drainage as well as damage to retinal ganglion cells and associated visual field losses. Consideration is given to the interaction between vascular and mechanical explanations for pathological changes in glaucoma. For example, elevated intraocular pressure (IOP) forces may contribute to ischaemia but there is increasing evidence that altered blood flow in a wider sense is also involved. Both vascular and mechanical theories are involved through fluctuations in intraocular pressure and dysregulation of blood flow. Retinal function is very sensitive to changes in haemoglobin oxygen concentration and the associated variations in the production of reactive oxygen species. Reperfusion injury and production of reactive oxygen species occurs when IOP is elevated or blood pressure is low and beyond the capacity for blood flow autoregulation to maintain appropriate oxygen concentration. Activities such as those associated with postural changes, muscular effort, eye wiping and rubbing which cause IOP fluctuation, may have significant vascular, mechanical, reperfusion and oxidative stress consequences. Hyperbaric oxygen therapy exposes the eye to increased oxygen concentration and the risk of oxidative damage in susceptible individuals. However, oxygen concentration in aqueous humour, and the risk of damage to trabecular meshwork cells may be greater if hyperbaric oxygen is delivered by a hood which exposes the anterior ocular surface to higher than normal oxygen levels. Oronasal mask delivery of hyperbaric oxygen therapy appears to be indicated in these cases.

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PALABRAS CLAVE
Glaucoma;
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Isquemia;
Lesión por reperfusión

Especies reactivas de oxígeno, estrés oxidativo, glaucoma y terapia de oxígeno hiperbárico

Resumen Esta revisión examina el papel del estrés oxidativo en el daño celular de la red trabecular, la disfunción del drenaje acuoso, así como las lesiones de las células ganglionares de la retina y las pérdidas de campo visual asociadas. Se tiene en cuenta la interacción entre las explicaciones a los cambios patológicos en el glaucoma, desde el punto de vista vascular y mecánico. Por ejemplo, la elevación de las fuerzas de la presión intraocular (PIO) puede contribuir a la isquemia, aunque existe evidencia creciente de que también está implicada la alteración del flujo sanguíneo, en un sentido más amplio. También están implicadas las teorías vasculares y mecánicas a través de las fluctuaciones de la PIO y la desregulación del flujo sanguíneo. La función de la retina es muy sensible a los cambios de la concentración de oxígeno en la hemoglobina y a las variaciones asociadas a la producción de especies reactivas de oxígeno. Las lesiones por reperfusión y la producción de especies reactivas de oxígeno se producen cuando la PIO es elevada o cuando la presión sanguínea es baja, y sobrepasa la capacidad de autoregulación del flujo sanguíneo para mantener la concentración de oxígeno adecuada. Las actividades tales como las asociadas a cambios posturales, esfuerzo muscular, lavado y frotamiento de ojos, que causan fluctuación de la PIO, pueden tener repercusiones considerables de tipo vascular y mecánico, y de reperfusión y estrés oxidativo. La terapia de oxígeno hiperbárico expone al ojo a un incremento de la concentración de oxígeno y al riesgo de daño oxidativo en individuos susceptibles. Sin embargo, la concentración de oxígeno en el humour acuoso y el riesgo de lesiones de las células de la red trabecular pueden ser superiores cuando el oxígeno hiperbárico es liberado por una campana que expone la superficie ocular anterior a unos niveles de oxígeno más elevados de lo normal. La liberación de oxígeno hiperbárico mediante mascarilla oronasal parece más indicada en estos casos.

The glaucomas are a worldwide leading cause of irreversible vision loss.[1] They can be viewed as neurodegenerative diseases which, like other conditions such as Alzheimer's or Parkinson's disease, are ultimately caused by deficits in neuronal function.[2] For example, the glaucomas are characterised by progressive degeneration of retinal ganglion cells (RGC)[1] and their axons.[3] As RGCs cannot divide or regenerate, optic nerve damage appears to be irreversible.[3] The molecular basis for RGC death is complex and includes axonal transport failure, neurotrophic factor deprivation and oxidative stress, for example.[2] It is likely that several molecular pathways converge to induce RGC loss.[2]

Mechanical and vascular explanations for glaucomatous pathology

According to the mechanical theory of glaucoma, increased intraocular pressure (IOP) can be a consequence of abnormal resistance to aqueous humour drainage via the trabecular meshwork.[4] The mechanical theory stresses the importance of direct IOP-related increased compression of the axonal fibres and support structures of the anterior optic nerve, with distortion of the lamina cribrosa plates and interruption of axoplasmic flow, resulting in death of the RGCs.[5] Compression of the anterior optic nerve is also a function of intracranial pressure which may vary in concert with, or independently of IOP fluctuations.[6] However, apart from mechanical stress elevated IOP-related factors also trigger initial neuronal damage in glaucoma through ischaemic injury processes.[6,7] The vascular theory focuses on the development of intraneural ischaemia resulting from decreased optic nerve perfusion.[5] Causes of decreased blood flow include mechanical compression of vessel walls,[8] for example. Mechanical stress could detrimentally affect blood supply to the laminar segments of the axons through deformation of the capillary-containing laminar beams.[9] This model is consistent with the results of Gottanka and coauthors who found a loss of capillaries supplying the optic nerve (ON) in primary open angle glaucoma (POAG).[10]

However, there is increasing evidence that altered blood flow in a wider sense may play a major role in the pathogenesis of OAG.[11] Autoregulation is a manifestation of local blood flow regulation being the intrinsic ability of an organ to maintain a constant blood flow despite changes in perfusion pressure.[12] Vascular dysregulation interferes with autoregulation of ocular perfusion and renders the eye to be more sensitive to IOP elevation or blood pressure (BP) reduction.[13] Reduced blood circulation due to vascular dysregulation resulting from IOP fluctuation is more damaging than reduced circulation due to a stable elevated IOP or arteriosclerosis[13] because instability of ocular blood flow leads to reperfusion injury which is mild but

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