Macular Edema in Retinal Vein Occlusion: Expanding Therapeutic Targets

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Retinal vein occlusion (RVO) affects 16 million people worldwide and its prevalence increases due to the ageing of the population [1]. Likewise, management of this visually debilitating condition poses challenge taken into account its complicated etiopathogenesis. Despite improved treatment with intravitreal injections of antiangiogenics and intravitreal steroid implants, RVO is still associated with non-responders, tachyphylaxis, rebound phenomena, high re-injections rate, which may represent also a rising economic burden, non-feasibility of endless injections, thus underscoring the importance of addressing new approaches to formulate treatment strategies.

Vaso-occlusion of retinal vein represents a blockage and retardation of retinal venous drainage, manifesting by elevated intracapillary pressure, which causes the leakage of blood and fluid, specifically in the macular area resulting in macular edema and macular ischemia.

Macular edema is the leading cause of decreased central visual acuity in RVO. Longer duration of RVO-related macular edema is associated with poorer outcomes. Proposed mechanism of macular edema is based on the breakdown of the blood-retinal barrier as a consequence of multiple damaging factors, such as disturbed junctions between endothelial cells of capillaries, produced by retina vasoactive-factors increasing vessels permeability, vitreoretinal adhesions initiated by fluid extravasates into surrounding tissue following the Starling’s law. Tissue hypoxia due to primary venous occlusive disease is the most common driver of vascular endothelial growth factor (VEGF) synthesis, that is why suppression of overexpressed VEGF by anti-VEGF agents underscored their predictably rational use, specifically directed to reduce vascular permeability. Aforementioned initiated a common use of intravitreal injection of vascular endothelial growth factor inhibitors for RVO-related macular edema in recent years. Despite this impactful intervention, currently available findings obviate that pharmacotherapy by short acting antiangiogenics reached a physiological “ceiling” effect and symptomatic treatment intended to suppress just one chemical substance is inadequate to successful therapy of macular edema in RVO.

Ophthalmologists face a host of new challenges in the management of retinal venous occlusion as the natural history of the disease becomes better understood and new technologies become available. Scientific understanding of macular edema in RVO continues to develop, and recent changes have been made to underscore the other game players in such complex biological process as a macular edema, beyond anti-VEGF, which remains the important, but not the only process-driving factor. Recently, it was highlighted to be caused by different other inflammatory mediators (interleukins (IL-6, IL-8), monocyte chemoattractant protein-1, aqueous erythropoietin (EPO)) as a result of multiple inflammatory cascades [2].

This suggests a therapeutic potential of intravitreal steroid implants with multiple mechanism of actions, one of which is anti-inflammatory due to blockage of cytokine production and inhibition of leukocyte adhesion induced by VEGF-A, but a challenge is an invasive repeatable procedure accompanied by cataract formation and ocular hypertension.

The latest findings evidenced and clinically confirmed the multifactorial nature of Diabetic Macular Edema [3], which could be hypothetically adapted for RVO-related macular edema, suggesting universal pathogenic mechanisms in macular edema unrelated with its cause.

Today, there is also a need to focus not only on achieving the maximal efficacy of therapy, but at the same time to improve safety of proposed interventions: noninvasive approaches such as lacrimal plug, reduction of toxicity, ocular and systemic side effects; and likewise, to increase retinal bioavailability of novel pathogenetically-tailored therapeutic agents.

Developing an understanding of the pathophysiological mechanisms of macular edema in RVO will certainly allow the formulation and implementation of new, more effective, and safe therapeutic procedures, to provide novel treatments to our patients. Having an awareness of cutting-edge advances in the field can be key to millennial-minded approach for RVO-related macular edema management.

Bibliography

