EDITORIAL

Minimizing Proliferative Vitreoretinopathy Reaction in Rhegmatogenous Retinal Detachment: Is There a Role of Preoperative Anti-Inflammatory?

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Rhegmatogenous retinal detachment (RRD) is characterized by the detachment of the neurosensory retina from the retinal pigment epithelium (RPE). Delaying retinal surgery may trigger the formation of abnormal proliferative tissue from retinal cells and RPE tissue in the vitreous, known as proliferative vitreoretinopathy (PVR).[1,2] These complications have the potential to induce contraction, tractional force, and eventual retinal detachment. The progression of PVR involves intricate mechanisms influenced by inflammatory processes or mediators, angiogenesis, and fibrotic changes, contributing to the formation of new blood vessels and the deposition of connective tissue.[2,3,4,5,6]

The inflammatory response associated with PVR is characterized by elevated levels of arachidonic acid metabolites (PGE2 and COX- 2), TGF-ß, and monocytes or macrophages in the vitreous. Djatikusumo et al study scrutinized the preoperative administration of nepafenac 0.1%, a non-steroidal anti- inflammatory drug, aimed at averting the emergence of PVR in patients diagnosed with RRD, thereby enhancing the anatomical success of postoperative vitrectomy.[6,7,8]

The research constituted a randomized clinical trial involving 61 subjects, partitioned into two distinct groups: 31 participants in the nepafenac 0.1% group and 30 in the control arm. Inclusion criteria entailed patients diagnosed with RRD concomitant with PVR grade A or B, scheduled for pars plana vitrectomy (PPV) interventions. Vitreous samples were collected during vitrectomy, and the vitreous biomarker levels (PGE2, COX-2, TGF- ß, and monocytes) from each group were subjected to analysis.[7]

The administration of 0.1% nepafenac eye drops were administered three times daily for five days prior to PPV in patients with RRD and PVR. Evaluation was conducted to assess anatomical outcomes based on parameters including retinal reattachment rates, central subfield thickness (CST), and macular volume (MV). Overall, the study findings did not reveal a notable increase in anatomical success. Nonetheless, discernibly lower levels of TGF- ß, PGE2, and monocytes were observed in the 0.1% nepafenac group. Despite this observation, statistically insignificant differences were observed in biomarker levels between the two study groups.[7]

In physiological conditions, RPE cells exhibit a state of dormancy concerning mitotic activity. Conversely, in retinal conditions characterized by compromised blood barriers such as ischemic conditions, the pathophysiological state of photoreceptor cells in RRD within the vitreous cavity prompts an increase in chemotactic and mitogenic activity. This condition initiates a cascade of inflammatory reactions, yielding various growth factors, cytokines, and chemokines, thereby fostering the proliferation and transformation of EPR cells. In PVR, as a pathological response, EPR cells transform into fibroblast-like cells, inducing functional and

structural alterations characterized by the expression of alpha- smooth muscle actin responsible for contraction, glial fibrillary acidic protein (GFAP), and vimentin, which serve as the primary components of the epiretinal membrane.[9]

The proliferation of myofibroblast cells contributes to the formation of an extracellular matrix, leading to the development of peri- retinal membranes capable of contraction, termed as proliferative vitreoretinopathy (PVR). Clinically, PVR is characterized by the presence of fibrous tissue membrane proliferation on the retinal surface (epiretinal), within the retina (intra-retina), or beneath the retina (sub-retina). As the condition progresses, these membranes undergo contraction, thereby exacerbating the severity of RRD.[1,2]

The definitive management of RRD remains immediate surgical intervention. Delaying definitive treatment poses a consequential risk of vision loss, as the success rate of surgery tends to decline with the severity of PVR. The anatomical success rate of surgery, in terms of restoring ocular structural integrity, has been reported to range between 60% to 80%, contingent upon the severity of PVR. However, achieving functional visual acuity, such as ambulatory visual capacity or finger counting visual acuity, is only attainable by a minority of patients, ranging from 40% to 80%. As of present, there is no consensus regarding the optimal timing for retinal surgery in cases of RRD.[10,11]

A variety of pharmacological interventions have been investigated in the quest for effective PVR management in RRD, each tailored to target diverse pathogenic mechanisms encompassing anti-inflammatory, anti-growth factor, antiproliferative, antineoplastic, and antioxidant agents. The exploration of non- steroidal anti-inflammatory drugs (NSAIDs) has been relatively limited. However, NSAID application as a therapy for ocular conditions, particularly in the posterior segment of the eye, has been long practiced. An example of such a recommendation involves its utilization as pre- operative treatment in the prevention of macular edema following cataract surgery.[5,12,13]

This recent study contributes to understanding the role of vitreous biomarkers, particularly inflammatory factors, in elucidating the pathogenesis of PVR as a secondary condition or complication of RRD. Moreover, while retinal surgical intervention remains the definitive management for RRD cases, the potential of pre-vitrectomy nepafenac 0.1% administration unveils profound insights into the promising benefits of anti-inflammatory therapy in optimizing the management strategies for RRD.

The potential for preoperative interventions to mitigate the progression of PVR in RRD cases with delayed onsets, particularly in regions where vitreoretinal surgical resources are scant, presents a compelling avenue for investigation. Widjaja et al. study elucidated that the distance patients traveled to reach the referral hospital correlated with a prolonged duration from the onset of RRD symptoms to consultation. The extended onset-to-consultation period, especially spanning 31-60 days, exhibited a direct association with the severity of PVR. In Indonesia, there are currently only 162 vitreoretinal (VR) surgeons [InaVRS-Perdami 2023, personal communication], underscoring the limited availability of VR surgical resources in the country. Given this constraint, further exploration into alternative interventions beyond surgical management to mitigate PVR development before surgery, especially in locales where vitreoretinal surgical resources are sparse, offers a promising trajectory for elucidating comprehensive rhegmatogenous retinal detachment (RRD) management.[14]

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