

POSTERIOR VITREOUS DETACHMENT AND PHARMACOLOGIC VITREOLYSIS: THE NEW AGE OF ENZYMATIC VITRECTOMY

DESPRENDIMIENTO DEL VÍTREO POSTERIOR Y VITREOLISIS FARMACOLÓGICA: LA NUEVA ERA DE LA VITRECTOMÍA ENZIMÁTICA

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Posterior vitreous detachment (PVD) is a degenerative process in which the posterior hyaloid and the vitreous cortex detaches from the retina in association with a vitreous gel which is generally in a progressive liquefaction process. It is a senile process, which can be considered to be almost physiological with age and a lot more frequent in myopics. Postmortem studies have demonstrated that between 80 and 90 years of age, over 50% of the vitreous gel is liquefied. An additional factor involved seems to be the high intake of vitamin B6 as well as menopause, because synthesis and metabolism of proteoglycans of the vitreous is regulated by sexual hormones, with high estrogen levels acting as a PVD protecting factor (1).

A lot more is known about the ultrastructure of the vitreous than its metabolism. Studies by Sebag (2) proved that the vitreous gel is 98% water. It's most important macromolecules of collagen and hyaluronic acid, which gives it its three dimensional structure, together with glycoproteins and other molecules. Hyaluronic acid has a large hydrating capacity, which mainly account for the viscosity of this gel. Both hyaluronic acid and collagen —mainly collagen type 2— concentrate in the peripheral area of the vitreous, or cortex. Therefore, the vitreous cortex is more dense and consistent than the central region. The vitreoretinal interface, the virtual area of adhesion between the retina internal limiting membrane, and the posterior hyaloid which limits the vitreous cortex, is mainly maintained by fibronectin, laminin and collagen type 4 molecules, which perform as a sort of biological glue.

Fine and Spaide (3), in proving the existence of a precortical vitreous pocket and internal communication channels traversed by drugs such as triamcinolone, anti-VEGF and other antibiotics after intravitreal injection on their way to the macula, confirmed the classic theoretical schemes of the premacular bursa.

The metabolism of the vitreous remained largely unknown. The role played by hyalocytes in the vitreous is not clear: with functional characteristics as macrophages, fibrinolytic activity and contraction of the vitreous collagen, they are directly involved in maintaining the vitreous clear and avascularized, and very likely also in the appearance of PVD. Some procollagen molecules which are produced naturally at the level of the vitreous continue segregating after a vitrectomy, which would partially explain the re proliferation of membranes or the persistence of macular edema or incomplete closures of macular holes in spite of having carried out a vitrectomy, including peeling of the internal limiting membrane (4).

However, what is the use of the vitreous? the perverse effect of the vitreous remaining strongly adhered to, the retina is universally known, and it would be desirable for it to detach previously in a slow, progressive and controlled manner: 1) Post-retinal detachment relapses with or without vitreoretinal proliferation. 2) retinal detachment in pathologies with organized vitreous —Stickler syndrome, etc.— 3) Bilateralization of giant tears 4) Persistence and c, macular edemas (diabetics, venous occlusion, uveitis, pseudo-phakic Irvine-

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Gass syndrome). 5) myopic macular traction syndrome. 6) macular epiretinal membrane 6) appearance of macular holes and their progression from incomplete to complete. 7) progression of proliferative diabetic retinopathy, due to vitreous traction of the new vessels. The above are examples of the «goodness» and prophylactic effect of «suffering» PVD as early as possible.

However, the «good» PVD is also the physiopathological cause of severe pathologies such as regmatogenous retinal detachment or the worsening of existing ones such as the transformation of an incomplete, macular hole to a complete one, or a cystoid macular edema into a lamellar macular hole.

The suddenly symptomatic PVD, a pathology commonly associated to the «sudden increase of flies in the air» associates in almost 2- 5% of cases a retinal tear if we have enough patience to dilate the patient and make a detailed 360° exploration of the retinal periphery, under biomicroscopy. On the other hand, all patients with unilateral PVD must be warned about the risk of appearance in the contralateral eye within a short term: from 25% in the first year up to over 90% within three years. The literature shows that a prophylactic treatment of «non-symptomatic predisposing» lesions of the retinal periphery is not proved or universally accepted (4,5).

In short, the idea that a minimally invasive and low risk prophylactic and therapeutic action «inducing the artificial appearance of a PVD in a controlled manner», has gradually gained clinical possibilities, which gave rise to other wonderful idea of utilizing the LASIK suction ring to induce it (6) or the concept of pharmacological vitreolysis of the human vitreous. Therefore, pharmacological vitreolysis is considered to be a therapeutic option, which aims at a clinical alteration of the vitreous structure and a weakening of the vitreoretinal adhesion in order to produce a safe detachment of the posterior vitreous from the internal retina (7).

Several proteolytic drugs have been tried, to counteract the main components of the vitreoretinal adhesion with direct or indirect enzymatic capacity in order to degrade the substances involved in the maintenance of the vitreous collagen extracellular

structure and matrix which accelerate the liquefaction thereof, such as dispase, hyaluronidase, chondroitinase, plasminogen tissue activator, urokinase, streptokinase, natokinase, collagenase, plasmin and microplasmine (8).

Natokinase (Subtisilin NAT®), hyaluronidase (Vitrace®) and microplasmine (Trombogenic®). In stage two and three of clinical essay and presumably subsequent marketing. Of all said substances, plasmin is the most studied. Plasmin is a protease which can be isolated from the patient's serum and has been used as coadjuvant 15 minutes before surgical vitrectomy to facilitate surgery of macular holes and diabetic macular edemas. One of the main problems for its use is its lack of stability in addition to its high cost, laborious and sophisticated preparation technique.

If the above method is clinically developed, i.e., it manages to detached and liquefy the vitreous with a simple intravitreal injection, in the not too distant future we may witness an important change of paradigm in our current conception of vitreous surgery, that is the advent of enzymatic vitrectomy.

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