Letter to the Editor

Cyclooxygenases inhibitors for preventing the proliferative vitreoretinopathy: Ready for clinical use?☆

Inhibidores de ciclooxigenasa para impedir la vitreorretinopatía proliferativa: ¿aptos para uso clínico?

Dear Editor:

Proliferative vitreoretinopathy (PVR) is one of the main reasons for the failure of retinal reattachment surgery. PVR develops in 5–10% of reparative eye surgeries for retinal detachment, particularly surgical procedures performed on the inflamed or traumatic eye. The incidence of PVR after traumatic eye injury is estimated to be approximately 45%. PVR is associated with poor vision and blindness in the affected eye. It is assumed that PVR is a reparative process that is initiated by retinal breakdowns and extreme intraocular inflammatory reaction. High levels of intraocular inflammation lead to the development and contraction of cellular membranes within the retina, posterior hyaloid and retinal surface. These processes initiate a vicious cycle of retinal break, inflammation, transforming growth factor, the proliferation of the migrating cells, contractile myofibroblasts, and scar modulation. Therefore, most of the current treatments are based on reducing the level of intraocular inflammation to block cellular proliferation. Reoperation is a well-proven intervention to treat PVR associated retinal detachment; however, the recurrent rate is about 30% during the first months after surgery and the rate of surgery success is lower in cases of severe PVR.

Several pharmacological and non–pharmacological interventions have shown potential benefit for reducing the risk of PVR including, but not limited to, vitrectomy, 5-fluorouracil, oral 13-cis-retinoic acid, colchicine, low molecular weight heparin, curcumin, daunomycin, bevacizumab, and steroids. Steroids are among the most currently used therapies for preventing the incidence of PVR at the time of surgery. The mechanisms of action of these drugs especially the COX-2 inhibitors are multidirectional and complex; however, one of their main mechanisms is inhibiting the intraocular inflammatory reaction.

However, a result of a systematic review including three moderate-quality clinical trials showed that steroids might reduce the incidence of postoperative PVR grade B without affecting the visual acuity and retinal reoperation rate. In addition, these drugs fail to reduce the incidence of grade C of PVR. Furthermore, steroids can increase intraocular pressure and induce subcapsular cataract. Accordingly, finding safe drugs to prevent this complication is essential.

Recently, promising results of an animal study showed that lornoxicam intraperitoneal 230 mcg/kg could inhibit the formation of intra-vitreal and peri-retinal membranes up to 43% by blocking cyclooxygenases, such that the thickness of retinal and choroidal layers of the eye in the experimental group was similar to those of intact rats. The experimental models used in that study involved the dispase and the concanavalin model of PVR. For modeling rhegmatogenous retinal detachment, intravitreal injections were made below of the pars plana, then the fundus of injected animals was examined at days 1, 3, 7 and 42/56 after injections using a cine-recording ophthalmoscope. After that, the morphological evaluation was performed in the central retina. Edema, apoptosis, death of photoreceptor and retinal ganglion cells and proliferation of glial cells were considered as the early stages of PVR development. By these experiments, the authors found that although lornoxicam had no effect on the frequency of cataract appearance, it could diminish the incidence of vitreous hemorrhage and the development of endophthalmitis in concanavalin and dispase model of PVR, respectively. In addition, lornoxicam

☆ Please cite this article as: Jalalifar S. Inhibidores de ciclooxigenasa para impedir la vitreorretinopatía proliferativa: ¿aptos para uso clínico? Arch Soc Esp Oftalmol. 2019;94:e63–e64.
prevented the retinal and choroidal thickness changes during the development of PVR and reduced the frequency of membrane development, in both models. It should be noted that lornoxicam increased the incidence of endophthalmitis in the dispase model. Lornoxicam can inhibit the COXs and down-regulate the synthesis of these enzymes which suppress the intraocular inflammatory reaction. Accordingly, the results of that study are promising; however, future studies need to focus on the most useful cyclooxygenases inhibitor drug, its optimal dosing as well as its best route, duration and time of administration. In addition, although a number of approaches have been developed for the prevention and treatment of PVR, there is currently no consensus guideline regarding the optimal preventive approaches for the development of PVR. Since PVR is a critical ophthalmologic problem, more research should be conducted to target the inhibition of pathologic responses that underlie retinal membrane contraction. In addition, those interventions with promising results on animals, such as cyclooxygenases inhibitors should be tested on humans. The prevalence of PVR in rheumatologically patients with retinal detachment treated with COX inhibitors might be a good basis for further extended research.

REFERENCES


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