

A Sub-Conjunctiva Injection of Rosiglitazone for Anti-Fibrosis Treatment after Glaucoma Filtration Surgery

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Abstract : Trans-differentiation of human Tenon fibroblasts (HTFs) to myo-fibroblasts and fibrosis of episcleral tissue are the most common reasons for the failure of glaucoma filtration surgery, with limited treatment options like antimetabolites which always have side-effects such as leakage of filter bulb, infection, hypotony, and endophthalmitis. Rosiglitazone, a specific thiazolidinedione is a synthetic high-affinity ligand for PPAR- γ , which has been used in the treatment of type2 diabetes, and found to have pleiotropic functions against inflammatory response, cell proliferation and tissue fibrosis and to benefit to a variety of diseases in animal myocardium models, steatohepatitis models, etc. Here, in vitro we cultured primary HTFs and stimulated with TGF- β to induced myofibroblastic, then treated cells with Rosiglitazone to assess for fibrogenic response. In vivo, we used rabbit glaucoma model to establish the formation of post- trabeculectomy scarring. Then we administered subconjunctival injection with Rosiglitazone beside the filtering bleb, later protein, mRNA and immunofluorescence of fibrogenic markers are checked, and filtering bleb condition was measured. In vitro, we found Rosiglitazone could suppressed proliferation and migration of fibroblasts through macroautophagy via TGF- β /Smad signaling pathway. In vivo, on postoperative day 28, the mean number of fibroblasts in Rosiglitazone injection group was significantly the lowest and had the least collagen content and connective tissue growth factor. Rosiglitazone effectively controlled human and rabbit fibroblasts in vivo and in vitro. Its subconjunctiva application may represent an effective, new avenue for the prevention of scarring after glaucoma surgery.

Keywords : fibrosis, glaucoma, macroautophagy, rosiglitazone

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