PROLONGATION OF IMMUNOSUPRESSANTS DELIVERY FOR WOUND HEALING MODULATION IN GLAUCOMA SURGERY: EXPERIMENTAL IN VITRO STUDY

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PURPOSE: to develop a method to prolong delivery of selective immunosupressants in the surgery area for wound healing modulation in glaucoma interventions.

METHODS: we analyzed the ability of poly(lactic-co-glycolic) acid glaucoma drainage samples (Fig. 1) to cumulate cyclosporine A (CsA) from solutions with decreasing drug concentrations from 50,0 to 1,0 mg/ml for 5-60 minutes. Other drainage samples were enriched with everolimus with the help of ultrasound. Then drainage samples were lyophilized and amount of incorporated immunosupressants was evaluated by means of chromatography-mass spectrometry. The dynamics of immunosupressants desorption was analyzed in vitro: drainage samples enriched with CsA and everolimus were placed in containers with 9 ml balanced salt solution and kept at constant temperature 37 C° in a shaker (50-100 rpm). At specific times from 12 hours to 14 days drainage samples were removed from the solutions and residual content of the drugs was evaluated by means of chromatography-mass spectrometry.

RESULTS: poly(lactic-co-glycolic) acid glaucoma drainage turned out to be a good substrate for enrichment with both immunosupressants. It incorporated 3,87 μg of CsA and 240 μg of everolimus. Drainage samples released therapeutic concentrations of CsA for 7±0,5 days and everolimus for 12,0±0,8 days (Fig. 2).

CONCLUSION: we developed a method to maintain therapeutic concentrations of CsA and everolimus in vitro in close to real conditions for a period of time long enough to overlap the moment when T-cells and macrophages reach their peak amount and trigger fibroblast proliferation. Implantation of glaucoma drainages enriched with selective immunosupressants can potentially modulate wound healing in glaucoma surgery.

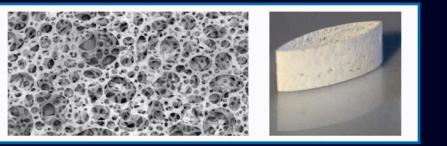

Fig. 1. Macro- and microstructure of glaucoma poly(lactic-co-glicolic) acid glaucoma drainage

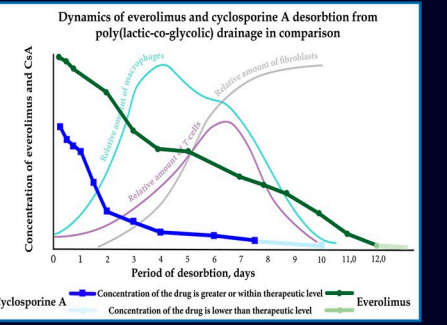

Fig. 2. Relationship between drug concentrationes released from glaucoma drainage and key participants of inflammatory-proliferation cascade