THE EFFECT OF MICROPLASMIN ON THE WOUND HEALING AFTER TRABECULECTOMY

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BACKGROUND AND AIM

Glaucoma is a progressive neuropathy of the optic nerve. The main cause of glaucoma is an elevated intra-ocular pressure (IOP). The treatment of this disease is directed towards the sustained reduction of IOP. Of all currently used treatments to lower IOP, filtration surgery (trabeculectomy) was shown to be the most effective. However, in 30% of the cases the constructed channel (bleb) closes due to excessive scar formation, resulting in surgical failure. (1) The four important processes contributing to post-operative conjunctival scarring are: clot formation, inflammation, angiogenesis and fibrosis.
Microplasmin (*Thrombogenics*) is a recombinant protein that dissolves clot and fibrin. Recently, Microplasmin has been shown to be efficient, well tolerated and safe for intra-ocular use in a phase III clinical trial to study its efficacy to induce non-surgical posterior vitreous separation.
The aim of our project is to investigate whether the administration of Microplasmin, a recombinant protein that dissolves clot and fibrin, could lead to a better maintenance of the constructed channel, and thus improve surgical outcome after trabeculectomy.

METHODS AND MATERIAL

The effect of Microplasmin will be investigated *in vivo* in a mouse model for conjunctival fibrosis and in a rabbit model for glaucoma surgery. Animals' postoperative follow-up will take place daily during the first week and two daily until they will be sacrified. Clinical investigation will be performed by measuring intraocular pressure, bleb area, and side effects on slit lamp examination. Moreover, (immuno-)histochemical analysis of the eyes will be performed by quantification of inflammation (CD45) and collagen deposition (Trichrome and Sirius Red.

In the first preliminary experiments in rabbits, topical Microplasmin drops was investigated *in vivo* in a rabbit model for glaucoma surgery. In the first experiment, topical Microplasmin drops were compared to placebo drops (n=3). In the second experiment (n=5), subconjunctival Microplasmin injection was compared to placebo injection. In the third experiment (n=10), intracameral Microplasmin injection was compared to placebo injection. In the last experiment a combination of intracameral Microplasmin and topical drops was compared to placebo injection and drops. All experiments were conducted by a masked observer. The aqueous solution of Microplasmin used in all experiments was not optimized for use as drops or in subconjunctival injection.

These preliminary experiments showed that Microplasmin combination therapy significantly augmented the bleb area over the 30 days of follow-up (p=0.05). There was a trend that the single anterior chamber injection augmented the bleb area in the first week compared to control (p= 0.08). In contrast the beneficial effects of Microplasmin after topical administration alone or subconjunctival Microplasmin tra-

beculectomy were absent (p=0.73, 0.90 respectively). No significant changes in collagen deposition and inflammation in the anterior chamber or in the conjunctiva were noticed. There is a need for larger groups, to optimalize the formulation of Microplasmin, to try repeated injections and to unravel the working mechanism of Microplasmin.

CONCLUSION

The combination of anterior chamber injection and topical drops improved surgical outcome of trabeculectomy in a rabbit model. Our proposed research will elucidate the potential role of Microplasmin in the improvement of filtration surgery outcome, and will highlight any anti-clotting, anti-inflammatory, and/or anti-fibrotic effects of this molecule.

REFERENCES

(1) ADDICKS E.M., QUIGLEY H.A., GREEN W.R et al. – Histologic characteristics of filtering blebs in glaucomatous eyes. Arch Ophthalmol. 1983; 101: 795-798.