MICROPLASMIN AS AN ANTISCARRING AGENT FOR GLAUCOMA SURGERY: TRANSLATION INTO CLINICAL APPLICATION

VANDEWALLE E., VAN BERGEN T., VAN DE VEIRE S., MOONS L., STALMANS I.

Affiliation Institution: KULeuven, UZLeuven

Promotor of the Project: STALMANS I., MD, PhD

BACKGROUND AND AIMS

The effect of Microplasmin was investigated *in vivo* in a rabbit model for glaucoma surgery. Microplasmin combination therapy 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 trabeculectomy were absent ($p=0.73$, 0.90 respectively).

The aqueous solution of Microplasmin used in all experiments was not optimized for use as drops or injections. Microplasmin is an autocatalytic enzyme which has a short half life when it is brought in conditions of 37 °C and physiological pH. Therefore there is need for a more stable and longer acting formulation of Microplasmin.

This project will focus on the further development of Microplasmin as an antiscarring agent for glaucoma surgery by 1. Optimizing the formulation of Microplasmin for extended drug delivery
2. Optimizing the route and regiment of administration.

DEVELOPMENT OF THE PROJECT

This project will be conducted in collaboration with the laboratory of pharmaceutical technology and biopharmacy of Prof Dr. A. Ludwig of the University of Antwerp. Prof Ludwig and her team have a great expertise in developing sustained release products for ocular use. This expertise will be of utmost importance to optimize the formulation of Microplasmin.

There are many potential routes for local delivery of therapeutic molecules to the eye. For trabeculectomy, we can withhold 4 likely application methods: topical, in the fornix, subconjunctival and intracameral.

To increase the efficacy of topical drops, we need to prolong contact time between the drug and corneal/conjunctival epithelium. A first strategy is to increase the viscosity of the vehicle of eye drops by the use of viscolysers to create gels. Another approach is to optimize the dosage form by the implementation of mucoadhesive polymers. The use of films or inserts like a minitablet also allows longer drug release.

Then we need to add Microplasmin to our different administration routes and determine the activity profile of Microplasmin:

- Topical (postoperative drops)

- In the fornix (postoperative minitablets)
- Subconjunctival (peroperative gels)
- Intracameral (peroperative injection of solution or gel)
- Combination of peroperative and postoperative administration

We will determine the most suitable way to obtain a longer drug release as well as a good activity profile for Microplasmin.
This new concept of Microplasmin with extended drug release will be tested in our rabbit model for glaucoma surgery.

Our proposed research project will optimize the formulation of Microplasmin for extended drug delivery and determine the optimal administration route and regimen. Microplasmin as an adjuvant therapy in glaucoma surgery might open new perspectives for more efficient surgery.

REFERENCES

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