CAN PEROPERATIVE BEVACIZUMAB IMPROVE TRABECULECTOMY OUTCOME? "AVASTIN-TRAB STUDY"

VANDEWALLE E., SPIELBERG L., ZEYEN T., STALMANS I.

Affiliation Institution: Department of Ophthalmology, University of Leuven
Promotor of the Project: STALMANS I., M.D., PhD.

BACKGROUND AND AIM OF THE PROJECT

Glaucoma is a progressive neuropathy of the optic nerve. The main important modifiable risk factor 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.

We found that vascular endothelial growth factor (VEGF) was upregulated in the aqueous humor of glaucoma patients and in the rabbit model. VEGF stimulated fibroblast proliferation in vitro. This suggests that VEGF is involved in the scarring process after filtration surgery. Bevacizumab reduced the proliferation of fibroblasts in vitro and an intracameral injection postoperative improved the surgical outcome in a rabbit model. (2)

The aim of this project is to study whether peroperative intracameral bevacizumab (Avastin®) might improve the outcome of filtration surgery in glaucoma patients.

MATERIAL AND METHODS

This study will be carried out in a prospective, placebo-controlled, double-blinded experimental setup. The effect of peroperative administration of bevacizumab on intraocular pressure, bleb characteristics and post-operative medication and surgical intervention will be investigated. The risk of systemic side-effects will be minimalized by using local anti-VEGF treatment.

The study patients will be divided into two major groups: A) Patients with primary open angle glaucoma and B) Patients with normotensive glaucoma, in which very low IOPs are targeted. Both groups of patients will undergo a trabeculectomy. Patients in group A will not be given the antimetabolite Mitomycin C (MMC), while patients in group B will receive MMC to obtain sufficiently low IOPs. This strategy adheres to standard operating procedures for filtration surgery. Patients in groups A and B will each be further subdivided into two subgroups: patients in groups A1 and B1 will be treated peroperatively with the study medication (bevacizumab), while patients in groups A2 and B2 will be treated with the placebo (saline). The assignment to the subgroups will be done by the pharmacist who prepares the study medication, and will be masked to the investigators as well as to the study participants.

The university hospital pharmacy will be requested to provide the investigators with masked syringes of the study medication (bevacizumab) and placebo (saline), as well as a randomization
list. The concentration will be 25 mg/ml and the administered volume 50 micro liters.

Patients will be evaluated on the first two days after surgery, and subsequently on weeks 1, 2, 4 (+/-1), 8 (+/-1). After that, they will be ex-

amined every three months until one year after surgery.
The end of the study will be the last visit of the last subject undergoing the study. This will occur at 12 months after the surgical intervention of the last subject undergoing the study.

CONCLUSION

Our study will potentially shed new light on a plausible and simple method to improve the prognosis of glaucoma filtration surgery. Since this study will provide direct data on the effectiveness of a one-time treatment that might reduce the risk of bleb failure after filtration surgery, avoiding or reducing the need for long-term medication use or secondary surgical intervention, the potential clinical implications of this study are clear. Thus, our project opens exciting new perspectives for the treatment and prognosis of the blinding condition of glaucoma.

REFERENCES

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