Subconjuntival bevacizumab enhances the antifibrotic effect of MMC and allows to reduce its exposure time to improve safety
Tine Van Bergen¹, Evelien Vandewalle², Lieve Moons³, Ingeborg Stalmans¹ ²
¹Lab of Ophthalmology, KU Leuven, Leuven - Belgium
²Department of Ophthalmology, UZ Leuven, Leuven - Belgium
³Department of Biology, Zoological Institute, KU Leuven, Leuven - Belgium

Purpose: In this study, we first determined the most optimal administration route of bevacizumab after GFS. Secondly, we investigated whether reducing the exposure time and/or dose of MMC in combination with bevacizumab could improve surgical outcome with a lower incidence of side effects.

Methods: In the first experiment, mice were operated (n = 10/group) and received a subconjunctival (SC), intracameral (IC) or intravitreal (IV) injection of bevacizumab (1µl; 25 µg) or NaCl (1µl; 0.9%). Bevacizumab plasma levels were measured using ELISA (n = 3/group). In the second experiment, the combination of MMC and bevacizumab was compared to MMC monotherapy and NaCl in operated mice (n = 10/group). Surgical sponges soaked in MMC 0.02% and 0.01% were investigated and exposed to the sclera for 1 or 2 minutes. Treatment outcome was studied by clinical investigation of the bleb every other day until all blebs failed.

Results: Treatment using a SC, IC or IV bevacizumab equally improved surgical outcome compared to NaCl (p > 0.05). Importantly, bevacizumab was detected at relatively high levels in plasma shortly after IV injection (6.35 µg/ml after 30 minutes), whereas a minimal bevacizumab absorption was detected only from day 4 after SC (0.69 µg/ml) or IC (2.46 µg/ml) administration. Based on these results, SC injections were selected for the second experiment. Administration of SC bevacizumab combined with 1 or 2 minutes of MMC 0.02% equally improved bleb area and survival, as compared to MMC 0.02% alone (p > 0.05). The combination of bevacizumab and 1 minute exposure of MMC 0.01% also significantly improved surgical outcome (p < 0.001 versus 1 min MMC 0.01%), although to a lesser extent than the combination with MMC 0.02% for 1 minute (p < 0.001). Importantly, 25% of the eyes treated for 2 minutes with MMC showed corneal toxicity, whereas this was not the case after 1 minute of administration.

Conclusions: This study demonstrates that SC and IC injection of bevacizumab offer an effective way to improve surgical outcome after GFS, with less systemic absorption compared to IV injection. Moreover, adjunctive bevacizumab allows to reduce the administration time of MMC 0.02%, thereby eliminating its toxic effects on the cornea while maintaining the beneficial effects on surgical outcome.

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