

Preclinical Safety Evaluation of Intravitreal Injection of Full-length Humanized Rhumab Vascular Endothelial Growth Factor Antibody in Rabbit Eyes

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PURPOSE

Choroidal neovascular membrane, proliferative retinopathies and retinal vascular occlusions are caused by microvascular disability stimulated mainly with vascular endothelial growth factor (VEGF). Bevacizumab, as a full-length anti-VEGF, has been one of the treatment modalities. The current study was performed to investigate intraocular toxicity of the bevacizumab after intravitreal delivery.

METHODS

Twenty four rabbits were divided into two groups. First group (Group 1 and 2) received 1.25 mg (0.05 ml) intravitreal bevacizumab and the second group (Group 3 and 4) received 3.00 mg (1.2 ml). Right eyes assigned as study eyes while left eyes served as a control and received same volume of saline intravitreally. Group 1 and 3 were labeled as early group and scheduled to be terminated at 14th days. Groups 2 and 4 as late groups were scheduled to be ended at 28th days. Electroretinography (ERG), corneal thickness, intraocular pressure measurements were performed at baseline and scheduled time points. After the rabbits were sacrificed eyes were enucleated for light and electron microscopy.

RESULTS

No anterior segment inflammation was observed except one eye in the group 1 which showed uveitic findings that was subsided without treatment. No evidence of retinal toxicity was seen with intravitreal bevacizumab in the doses of 1.25 mg and 3.00 mg when tested by ERG findings. A and b wave amplitudes were not statistically significant before and after intravitreal bevacizumab injection in both doses at short and long term durations ($p > 0.05$). No abnormality was detected with VEP recording. Histopathology and electron microscopic findings showed normal retinal structure. Intraocular pressure was stable and crystalline lens remained clear. Other outcome measures showed no side effects in both doses at early and late time points. Uveitic reaction which may be dose independent.

CONCLUSION

Our study failed to demonstrate intravitreal bevacizumab related toxic side effects to the intraocular tissues including retina. Both electrophysiologic and histopathologic investigation showed normal retinal function and structure after both low and high dose treatment with bevacizumab. However, in clinical setting caution must be exerted for possible anterior uveitic reaction.