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Retina biocompatibility of novel vital dyes for chromovitrectomy

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Purpose: To investigate the retina biocompatibility of six novel vital dyes for chromovitrectomy in rabbits. Methods: A total of 60 rabbits were used to perform the experiments, and the study was conducted in compliance with the Declaration of Heisinki and the UNIFESP Ethical Committee. A total of 0.05 ml of 0.5 % and 0.05 % Light green (LG), Fast green (FG), Evans blue (EB), Brilliant blue (BriB), Bromophenol blue (BroB) or Indigo carmine (IC) were injected intravitreally into the right eye, while in the left eye 0.05ml of balanced salt solution (BSS) was applied for control. Fundus photograph, fluorescein angiography (FA), histology with light microscopy (LM) and transmission electron microscopy (TEM) were performed after one day and seven days. The retinal cellular layers were evaluated according to morphologic alterations and number of cell counting in three histology sections within an area of 1.500 microns by TEM and LM. The number of cells within the ganglion cells, bipolar cells, and photoreceptors were compared to the control eyes, statistic significance was considered for $p<0.05$ (Student's t-test). The electroretinographic changes were assessed at baseline, 24 hours and 7 days after intravitreal injection of 0.05% or 0.5% for each dye. Both latency and amplitude of maximum response, rod response, and oscillatory potentials were used for detection of functional signs of retinal toxicity. Results: Histology examination with LM and TEM disclosed only mild focal morphologic changes without loss of cellular elements in eyes exposed to 0.05% LG, IC, FG, BriB, and BroB, similar to the control group. Intravitreal injection of 0.05% EB induced statistically significant loss of cells in comparison to control by LM and TEM ($p<0.05$). At the higher dose of 0.5% BroB, LG and EB promoted diffuse cellular changes manifested as cellular edema and vacuolization within the ganglion and bipolar cells, whereas 0.5% FG and IC caused only mild retinal alterations similar to BSS injection. BriB at 0.5% induced overall no major retinal toxicity, however, focal changes in the photoreceptors have been observed. Intravitreal injection of 0.5% EB, LG, and BroB caused significant loss of neuroretinal cells in comparison to BSS-injected eyes ($p<0.05$). ERG examination revealed

prolonged latency and increased amplitude in eyes submitted to injection of 0.5% EB, LG and BroB. FA examination disclosed no clinical signs of outer retina toxicity such as hyperfluorescence due to RPE window defects. Conclusions: The vital dyes FG, LG, IC, BroB, and BriB at low dose 0.05% demonstrated no toxicity to the retina. However, at higher dose of 0.5% FG, IC, or BriB may be applied safely in chromovitrectomy.