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LETTER TO THE EDITOR (BY INVITATION)

Letter in response to letter: intraocular use of acid violet 17 at a concentration of 1.5 mg/ml is not safe

By Professor Heinrich Gerding, Department of Ophthalmology, Pallas Kliniken

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Dear Editor,

We thank Professor Gerding for his letter in response to our publication. We would like to point out that the study was performed and accepted for publication after the dye had been approved for human use and before it was withdrawn from the market. Our study was not connected with regulatory approval in any way. We investigated the dye for its staining properties and the induced cleavage plane of the internal limiting membrane (ILM) from the retina [1]. We also reported visual acuity outcomes which were no different from those found using Brilliant Blue G within the limitations of our experimental design. In the patients we treated, we did not observe any dye-related toxicity based on either vision, neurosensory retinal changes or retinal pigment epithelial alterations. Our ILM cleavage plane findings were also reassuring in this respect. We were concerned to hear of Professor Gerding's paper and, like all other responsible surgeons, stopped using the dye as soon as it was withdrawn from the market.

We agree with all the points made regarding the preclinical studies. Indeed, in our article we noted that inner retinal toxicity had been found at doses exceeding 0.125 mg/ml in bovine eyes [2] and that the marketed preparation had a concentration of 1.5 mg/ml. We hypothesised that our methodology of a short (10 s) contact time and the added mannitol may explain the lack of toxicity we observed. Other possibilities—which we acknowledge are pure postulation—include a short light exposure time and low illumination levels during peeling. We also avoided repeat staining after ILM peeling ('double staining'). We were careful in the manuscript to explain our exact methodology of dye application, which avoids the jetting of dye onto the macular area and hole itself, and which as the correspondent observes may also have an effect on the occurrence of toxicity.

We agree that a more vigorous approval process for dyes used during vitrectomy surgery should be considered by the regulatory bodies. This should include representative in vivo animal models using the concentrations and formulation as used in the marketed product. The tests should include the effects of light exposure during and after dye exposure, with direct dye–ILM contact without intervening vitreous for clinically realistic time periods. They should also evaluate the contact of dyes after ILM peeling on the exposed retinal nerve fibre layer, as double staining to check that all ILM has been peeled has been commonly described in surgical papers. Indeed, a wide safety margin should be adopted in these tests, given that post-marketing, surgical practices will vary.

It is important for all surgeons to be vigilant to the possibility of adverse reactions from products released after marketing approval. We were fortunate not to have experienced any with this particular product ourselves and acknowledge Professor Gerding's experiences.

Yours faithfully
David Steel

References

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