Sir,

Severe retinal damage after macular hole surgery with extensive indocyanine green-assisted internal limiting membrane peeling

Eye (2004) **18,** 538–539. doi:10.1038/sj.eye.6700698

Peeling of the internal limiting membrane (ILM) seems to be associated with a higher rate of closed macular holes and better visual outcomes in macular hole surgery.[1] Staining with indocyanine green (ICG) is used to improve the visualisation of the ILM intraoperatively, as the peeling of the ILM can be technically difficult.[2,3] However, there is an ongoing discussion if ICG might be toxic to the retina and the retinal pigment epithelium (RPE).

Case report

A 72-year-old male presented with reduced vision in his left eye (visual acuity 7/20). As a macular hole stage III was diagnosed, an operation for macular hole repair was recommended.

Operation procedure: subtotal vitrectomy using a xenon cold light fibre (Xenotron II, Geuder, Germany) optic was followed by a subcomplete fluid–air exchange. A volume of 1 ml of a 0.05% (0.5 mg/ml) solution of ICG was placed over the posterior pole for 5 min without using sclerotomy plugs. After an air–fluid exchange, the ILM was only slightly stained and the sight was reduced by a mild gas cataract. With the insufficiently stained ILM about 10–15 attempts were made to separate the ILM but only small parts of it were peeled which lasted about 10 min. A second application of ICG (0.5 mg/ml) in the fluid-filled eye for 2 min resulted in a better ILM staining and allowed for successful peeling. This was carried out within 3 min in an area of about two disc diameters around the macular hole which was then filled with a drop of autologous blood. After another fluid–air/SF6 exchange, the patient was told to keep a face-down position until the gas had resolved.

At 12 weeks postoperatively, the patient's visual acuity was reduced to recognition of hand movements with a large central scotoma (Figure 1). The macular hole was completely closed, but the fundus showed regional mottling of the posterior pole extending over an area corresponding to the previously peeled site (Figure 2).

Comment

In rats, intravitreal ICG causes morphological and functional damage to the retina.[4] There are also reports on possible retinal damage in humans after macular hole surgery,[5] and ICG staining may even have an adverse effect on functional outcome in macular pucker surgery.[6] An experimental application of ICG to the retina of human donor globes combined with illumination of different wavelengths showed structural changes of the ILM and the inner retina.[7] ICG might be toxic to the RPE and cause damage in the region of the macular hole, where it had

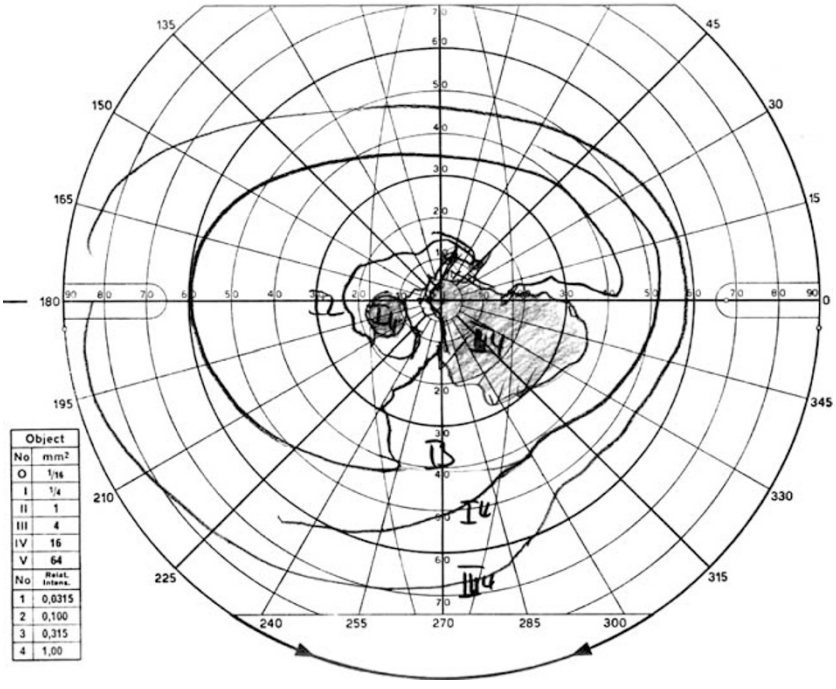

Figure 1 Goldmann visual field test showing a central and paracentral scotoma corresponding to the alteration of the posterior pole shown in Figure 2.

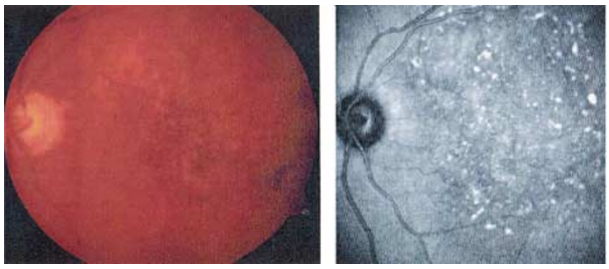

Figure 2 (1) Fundus photography of the posterior pole. Atrophic as well as hypertrophic changes of the retinal pigment epithelium are seen in a large area of the posterior pole, where peeling of the internal limiting membrane was performed after staining the internal limiting membrane twice with ICG. (2) Red free fundus photography of the same eye.

direct contact with the RPE.[8] In cell culture experiments, exposure of human RPE to ICG led to a decreased mitochondrial activity but not to changes in cellular morphology.[9] Stalmans *et al*[10] showed that this potential toxicity on cultured RPE is probably related to the hypoosmolarity of the ICG solution used for ILM peeling.

In our case, the concentration of ICG at the posterior pole was high due to staining under air with the solution being slightly hypo-osmotic (about 270 mosm/l). At the time of the second staining, small parts of the ILM may have been removed already, so that ICG had direct contact with the retina at these sites. However, the damage pattern did not correspond exactly to the ILM-free areas.

Additionally, the retinal damage could also be due to phototoxic effects enhanced by ICG.[7] Banker *et al*[11] report alterations of the RPE after macular hole repair without ICG, which were due to presumptive phototoxicity and associated with worse visual outcome.

Another explanation for the changes would be a prolonged and traumatic peeling procedure or a direct effect of the air–SF6 gas bubble combined with long-lasting postoperative face-down position, which sometimes might lead to a decrease in retinal perfusion pressure.[12] However, our case did not differ significantly from more than hundred uneventful preceding cases using ICG and gas endotamponade for macular hole repair carried out by the surgeon (LLH).

Potential toxic effects of ICG might be reduced by using low concentrations in iso-osmotic or viscoelastic solvents[3] or removing ICG shortly after installation in the liquid-filled eye. To decrease the risk of phototoxicity, the distance of the light source to the retina should be increased and the time of illumination during ICG staining should be minimised. Third, avoiding an overfill with gas would prevent reduced retinal perfusion and drying of the retinal surface. Keeping these limitations in mind, ICG remains a useful tool for ILM peeling in macular hole repair. It is, however, important to further investigate potential toxic effects of ICG.

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P Maier, LL Hansen and HT Agostini

University Eye Hospital, Killianstr. 5
79106 Freiburg, Germany

Correspondence: P Maier
Tel: +49 761 2704001
Fax: +49 761 2704057
E-mail: maierphi@aug.ukl.uni-freiburg.de