TOXICITY IS A QUESTION OF THE RELATIVE CONCENTRATION

THE APPLICATION OF INTRAVITAL DYES - THE CHROMOVITRECTOMY - HAS BECOME A FUNDAMENTAL ASPECT OF MODERN VITREORETINAL SURGERY.

In recent years, technological advances alongside better understanding of vitreoretinal pathophysiologies have aided to expand the areas of indication and goals for vitrectomy.

The indication of modern pars plana vitrectomy surgery frequently includes removal of transparent, epiretinal, membranous structures and/or the internal limiting membrane. The removal of these transparent structures demands for surgeon’s utmost abilities. To enable visualization of these transparent structures in order to be removed, indocyanine green (ICG) has been used “off-label” since 2000 as the first intraoperative dye for staining of the ILM. This dye derived from the photometric liver function diagnostics and fluorescein angiography. To date, it has not been yet approved for intraoperative uses in ophthalmic surgery. The use of ICG was controversially discussed due to clear signs of its toxic retinal side effects1-4, atrophies of the retinal pigment epithelium (RPE)5, damages to photoreceptors and RPE6,7, deteriorations of visual acuity8-13, loss of epiretinal cell integrity14 and cell toxicity15-20. Nine years later, in 2009, GEUDER/Flouron launched the first approved, non-toxic dosage dye21-25 for selective ILM staining: BrilliantPeel® (BrilliantBlue G – or Coomassie BrilliantBlue G). In following years, this triphenylmetane dye was combined with a neutral carrier in regards to physiological osmolarity (deuterium oxide) to ensure an optimal intraoperative subsidence and later complemented with an alternative, also in non-toxic concentration, ERM dye26-31 – Bromophenol Blue (BrilliantPeel® DualDye).

The currently available visualization options, ranging from the recently i-OCT, 3D Heads-up-Surgery, and a wide range of available dyes, equip surgeons with a broad spectrum of tools for imaging intraocular pathologies. The most accurate should always be the tool of choice since the classic toxicology maxim of Paracelsus: “All things are poison and nothing is without poison; only the dose makes a thing not a poison”21 remains valid. This applies to the amount of light introduced into the retina, as well as the components in dyes for intraocular use. The elements in dyeing agents can cause changes in the pH value or osmolarity, hence lead to critical disorders of retinal homeostasis, and even to toxic effects. Recent publications32 have investigated the influence of additives and the dosage form on the stability of such dyes, coming to the conclusion that - because of the reduced contact surface with air - prefilled syringes are preferable to vials in order to prevent oxidative degradation processes, when intended for intraocular dyes. The addition of preservatives can prevent such processes but may lead in some circumstances to extreme changes in the pH values.

Our recently published clinical observations34 suggest that the use of dyes for vitreoretinal surgery may be linked with unwanted, partly critical side effects, even in approved products. Besides unwanted staining of IOLs for up to 4 weeks postoperatively, we found, in an initially impressive intense staining on the ILM with the use of the dye Acid Violet17, surprising postoperative visual loss and massive structural damages on the retinal pigment epithelium in some patients with macular holes.

In summary, it can be affirmed that innovation cycles have shortened for chromovitrectomy, particularly heavy dies and combinations that stain ERM and ILM have become widely available, significantly improving visualization of vitreoretinal structures. Based on personal observation of undesired side effects with an already approved product, a sceptical attitude is recommended towards products with no long-term clinical data available. In our clinics, we are currently using as first choice a well-tried, yet innovative and recently improved product:
Brilliant Peel® Dual Dye. This combination dye for simultaneous staining of the ILM and ERM contains, besides the often used, extensively tested and proven Brilliant Blue G dye, a new addition Bromophenol Blue and the pH-neutral deuterium oxide as a carrier, and has a physiological osmolarity of 306 mOsm/kg H2O. In more than 60 applications we have achieved so far very satisfactory clinical results.