

Dyes for Internal Limiting Membrane Peeling: To Use or Not to Use?

BY ARTURO ALEZZANDRINI, MD; AND MARIO SARA VIA, MD

The internal limiting membrane (ILM) is a fine, multilaminar, semitransparent membrane 2.5- μ m thick. Its purpose is to act as a basal membrane for the Mueller cells, and it plays a main role in the pathogenesis of various vitreoretinal interface diseases, especially in the macular area.

The collagen in the ILM's structure provides the adherence surface for the hyaloid membrane under physiologic conditions. Under pathologic conditions, however, it acts as the foundation for fibrin and microfibroblasts to migrate. Microfibroblasts in particular, thanks to their contractile properties, produce wrinkling of the membrane, which alters the foveal surface and significantly reduces best corrected visual acuity (BCVA). Moreover, when the contraction produces tangential traction, it can lead to the production of macular holes.^{1,2}

Recent studies have suggested that the ILM has a main role in the development and treatment resistance of diffuse diabetic macular edema, as it thickens almost three times its normal size. It also plays an important part in macular edema secondary to central retinal vein and branch vein occlusion (Table 1).³ According to our own and other authors' experiences, surgical removal of the ILM in these conditions has proven to be effective in anatomic and functional improvements. The main technical difficulty is to remove and peel the membrane completely because it is transparent and multilaminar, making visualization challenging.⁴

In response to this difficulty, several techniques and new surgical instruments have been described in recent years. In our hands, the introduction of dyeing techniques has brought a significant improvement in the visualization and consequent extraction of the membrane.

The objective of this report is to demonstrate the



Figure 1. Intravitreal triamcinolone acetate facilitates visualization of the posterior hyaloid.

benefits of the use of dyes for ILM peeling during vitreoretinal surgery.

SURGICAL TECHNIQUE

We prefer to perform microincisional vitrectomy surgery (MIVS) with 23- or 25-gauge instrumentation. Once the trocars are introduced, we perform central and peripheral vitrectomy using panoramic lenses that allow easier peripheral manipulation of the vitreous. Once the vitrectomy is completed, mechanical aspiration enables the separation of the posterior hyaloid.

In young patients or patients with diabetes, we

TABLE 1. INDICATIONS FOR ILM PEELING

- Macular Holes
- Epiretinal Membranes
- Diabetic Macular Edema
- Macular Edema in CVO and BVO

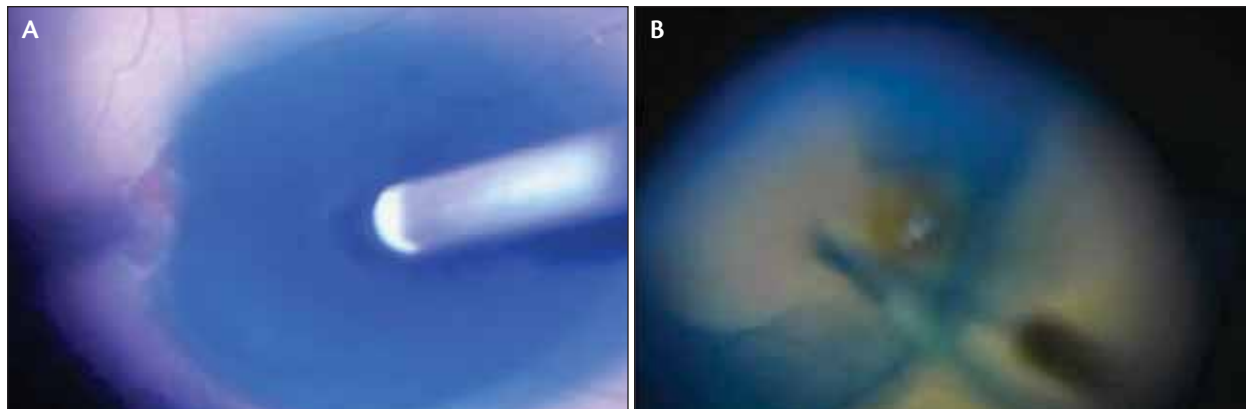


Figure 2. Brilliant blue G is injected over the macular area.

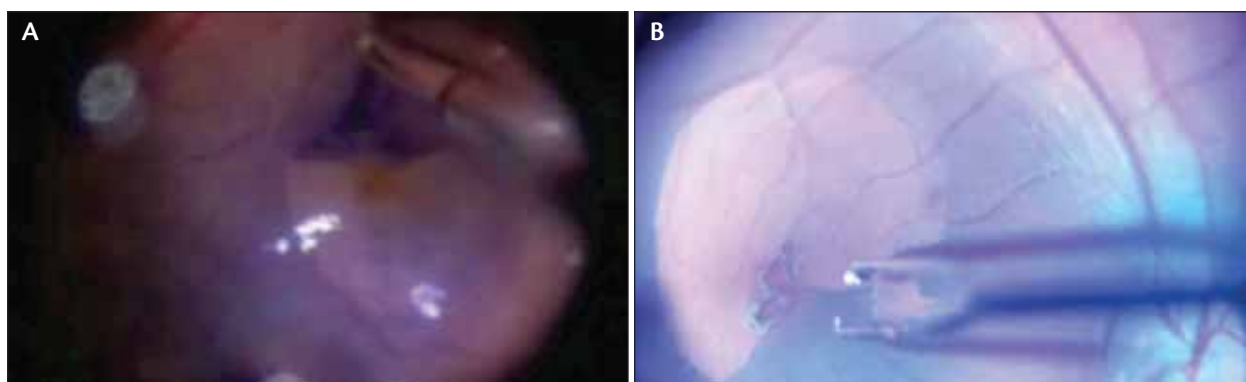


Figure 3. The maculorrhexis extension should not exceed the vascular arcade.

often use intravitreal triamcinolone acetonide, which facilitates the visualization of the posterior hyaloid and vitreous (Figure 1).

To improve visualization of the ILM, we use brilliant blue G (Brilliant Peel; Fluoron/Geuder, Ulm, Germany) dye. Depending on the trocar caliber we are using, we inject the dye with a 23- or 25-gauge straight cannula. The dye is injected over the macular area, without the need of performing a fluid-air exchange (Figure 2).

We use 0.25 mg/mL brilliant blue G in balanced salt iso-osmolar solution.

After a 45-second wait, we extract the dye by active aspiration and proceed to peel the ILM. For this we use ILM forceps (Grieshaber ILM Forceps with Revolution Grip, Alcon Laboratories, Inc., Fort Worth, TX). We look for an edge in the temporal foveal area, and in a concentric movement pulling inward we perform the maculorrhexis, pulling the ILM flap very carefully.

The maculorrhexis extension should not exceed the vascular arcade, and it is important to try to perform the peeling in only one maneuver (Figure 3).

We always perform a second dyeing followed by a second peeling, for ILM remnants may cause secondary traction and reopening of the macular hole postoperatively.

We finish surgery by performing a fluid-air exchange and, depending on the pathology, injection of gas into the vitreous cavity.

BRILLIANT BLUE G

We use brilliant blue G, more frequently than any other dye (Figure 4).

TABLE 2. ADVANTAGES OF PEELING ILM WITH BRILLIANT BLUE G

- Non toxic dye
- Easy to handle
- Great affinity for ILM
- Absence of phototoxicity
- Does not require fluid-gas exchange



Figure 4. Brilliant blue G.

The use of brilliant blue G was introduced by Enaida et al in 2006,⁵ when they showed that this dye was not toxic, either in vivo or in vitro, to retinal cells. It consists of anionic aminotriarylmethane with 280 mOsm osmolarity, molecular weight of 854, and a 7.4 pH.⁶

Brilliant blue G is a safe colorant to dye the ILM. No dose-dependent or time-dependent toxicity has been directly linked to its use. As it has great affinity for the ILM, it is easy to use at low concentrations and obviates the need for fluid-air exchange (Table 2).⁷⁻⁹

SPECIAL CONSIDERATIONS

ILM visualization without the aid of any dye is difficult, as the ILM is a semitransparent membrane and easy to identify only in highly pigmented eyes. Therefore, several dyes have been introduced to facilitate its visualization during surgery.

It is our opinion that to blame a BCVA decrease solely on the toxicity of the dye during the surgery would be an oversimplification.

Several reports describe the toxicity of the various dyes used in vitrectomy, and among them brilliant blue G seems to be one the most innocuous. Animal testing, in which the retina was exposed to the dye for long periods of time, showed only small alterations in the retinal cells. As far as our personal experience demonstrates, we have no evidence that brilliant blue G used for short periods of time during vitreoretinal surgery produces any structural or functional damage.^{10,11}

Toxicity of retinal dyes is difficult to evaluate based on BCVA after macular surgery because it depends on many factors such as the patients age, the severity of macular disease, and its time of appearance.

The surgical technique, the type of lighting, the distance of the light probe from the macula, and the time that the macula has been exposed are factors that also

affect the BCVA and retinal cell damage after surgery.

Mechanical damage, the type of instruments used to peel the ILM, the missed attempts to get ahold of it, and incomplete peeling of the membrane are also factors that can alter the final results apart from dye toxicity.

It is virtually impossible to distinguish which among all the factors described above is responsible for an unexpected drop in the patient's BCVA. In fact, it is our opinion that to blame a BCVA decrease solely on the toxicity of the dye used during the surgery would be an oversimplification.

It is our personal opinion as vitreoretinal surgeons that brilliant blue G allows us to identify and localize the ILM, and facilitates the grip of our instruments, reducing surgical time and retinal light exposure.

Although we cannot state conclusively that brilliant blue G is innocuous to humans, we suggest its use for vitreoretinal surgeries that require ILM peeling. ■

Arturo Alezzandrini, MD is with OFTALMOS, Instituto Oftalmológico de Alta Complejidad, Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina. Dr. Alezzandrini can be reached at +54 11 4812 1357; or via e-mail at aalezzandrini@oftalmos.com.



Mario Saravia, MD, is with Hospital Universitario Austral, Buenos Aires. Dr. Saravia can be reached at +54 23 22 48 2000; or via e-mail at mario.saravia@gmail.com.



The authors have no financial or proprietary interest in any of the products or techniques mentioned in this article.

- Rodriguez EB, Meyer CH, Farah ME, Kroll P. Intravitreal staining of the internal limiting membrane using indocyanine green in the treatment of macular holes. *Ophthalmologica*. 2005;219:251-262.
- Mester V, Kuhn F. Internal limiting membrane removal in the management of full-thickness macular holes. *Am J Ophthalmol*. 2000;129:769-777.
- Eckardt C, Eckardt U, Groos S, Luciano L, Reale E. [Removal of the Internal Limiting Membrane in macular holes. Clinical and morphological findings.] Article in German. *Ophthalmologie*. 1997;94:545-551.
- Lochhead J, Jones E, Chui D, et al. Outcome of ICG-assisted ILM peel in macular hole surgery. *Eye*. 2004; 18:804-808.
- Enaida H, Hisatomi T, Goto, Y, et al. Preclinical investigation of internal limiting membrane staining and peeling using intravitreal brilliant blue G. *Retina*. 2006;26:623-630.
- Enaida H, Hisatomi T, Goto, Y, et al. Brilliant Blue G selectively stains the internal limiting membrane/brilliant blue G-assisted membrane peeling. *Retina*. 2006;26:631-636.
- Malerbi F, Maia M, Farah ME, et al. Subretinal brilliant blue migration during epiretinal membrane peeling. *Br J Ophthalmol*. 2009;93:1687.
- Maia M, Penha F, Rodriguez EB, et al. Effects of subretinal injection of Patent Blue in rabbits. *Curr Eye Res*. 2007;32:309-317.
- Schumann RG, Remy M, Grueterich M, Gandorfer A, Haritoglou C. How it appears: electron microscopic evaluation of internal limiting membrane specimens obtained during brilliant blue G assisted macular hole surgery. *Br J Ophthalmol*. 2008; 92:330-331.
- Farah EM, Maia M, Rodriguez, E. Perspective dyes in ocular surgery: principles for use in chromovitrectomy. *Am J Ophthalmol*. 2009;148:332-340.
- Yuen D, Gonder J, Proulx A, Liu H, Hutnik C. Comparison of the in vitro safety of intraocular dyes using two retinal cell lines: a focus on brilliant blue G and indocyanine green. *Am J Ophthalmol*. 2009;147:251-259.