Autologous Serum Eye Drops for Treating Persistent Corneal Epithelial Defect After Vitreoretinal Surgery

To the Editor:

In the article by Oskouee et al,[1] the authors reported the use of bandage contact lenses and topical indomethacin to treat persistent corneal epithelial defects (PED) after vitreoretinal surgery. They suggested that monocular patients, patients who require rapid visual rehabilitation, and those who have discomfort when wearing patches would benefit greatly from treatment with a bandage contact lens. There are some points that I would like to add in this regard.

1. There are potential complications associated with using bandage contact lenses and topical nonsteroidal anti-inflammatory drugs. Cases of contact lens–induced corneal ulcers and nonsteroidal anti-inflammatory drug–induced delayed corneal reepithelialization and stromal melting have been reported.[2,3] Although the authors mentioned that no patients in their study developed a corneal ulcer and that all lesions healed by the sixth day, these complications have occurred in our hospital.
2. Patients who had vitreoretinal surgery complicated by PED usually had ocular surface problems or systemic diseases such as diabetes mellitus that might have predisposed them to infection. Hence, a method other than the bandage contact lens might be a better option for patients who develop PED after vitreoretinal surgery, especially monocular patients and those who require rapid visual rehabilitation.
3. Autologous serum is a safe and effective means of promoting epithelialization and has been indicated for the treatment of PED in several ocular surface disorders.[4,5] We also use autologous serum for patients who develop PED after vitreoretinal surgery. Previously, we used autologous serum eye drops for 3 patients who had no improvement with 2 weeks of conventional treatment, including bandage contact lens and nonpreservative artificial tears. All the lesions healed within 2 weeks. Because of the safety and efficacy, we now routinely use autologous serum if a vitreoretinal surgery–associated epithelial defect persists longer than 1 week. In our experience, most epithelial defects heal within 1 week.

Providing patients with better treatment is the duty and goal of physicians. We sincerely hope that topical autologous serum therapy will be considered for patients who develop PED after vitreoretinal surgery.

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Treatment of Persistent Corneal Epithelial Defects After Vitreoretinal Surgery: Autologous Serum Eye Drops or a Bandage Contact Lens?

Reply:

Huang et al have stated that the application of autologous serum eye drops is better than the application of a bandage contact lens and topical indomethacin for treating persistent corneal epithelial defects after vitreoretinal surgery.

Autologous serum eye drops have been used in the management of ocular surface diseases,[1] keratoconjunctivitis sicca,[2,3] dry eyes,[4,5] neurotrophic keratopathy,[6] persistent epithelial defects,[7] aniridic keratopathy,[8] and recurrent corneal erosions.[9] It has been reported that autologous serum accelerates epithelial healing and corneal epithelialization and decreases recurrent corneal erosions.[8]

Autologous serum has biochemical and biomechanical properties similar to those of normal tears, such as nonallergenic, antimicrobial, and optic properties. In addition, it contains epitheliotropic factors that are thought to be responsible for its therapeutic effect in ocular surface disorders. These factors include epidermal growth factor (EGF); basic fibroblast growth factor; vitamin A; fibronectin; α2-macroglobulin; and neural growth factors that facilitate the proliferation, migration, and adhesion of epithelial corneal cells. In addition, autologous serum facilitates mucin expression, which contributes to the beneficial effects on the ocular surface in patients with dry eyes.[8]

However, I would like to add some comments regarding the application of autologous serum eye drops.

1. Serum has multiple biologic factors that can affect the wound-healing process. For example, serum contains mitogenic factors for the corneal epithelium such as substance P[10,11]; extracellular matrix components (eg, fibronectin); growth factors that are responsible for the initial epithelial migration (eg, transforming growth factor-β and EGF) and mitosis (EGF)[1,7]; protease inhibitors; and antiapoptotic factors.[12] The relative contributions of these factors have not been determined although, overall, their combination in serum seems to have greater healing activity than conventional therapy.[13] It is still not clear whether it is better to prepare a special solution from autologous serum, with specific concentrations of such factors for each ocular surface

disorder, which has the desired effect, or to prepare a fixed solution with all these serum factors.
2. The method of preparing autologous serum has not been standardized, and the published protocols used to prepare serum vary widely. The optimal serum concentration, diluent, storage method, temperature, and dose frequency have not been established.[13] Schulze et al[14] used 50% serum diluted in balanced salt solution that was stored in a cool dark environment for up to 48 hours. The concentration of serum in reported studies ranged from 20% to 100%.[7]
3. Another major problem that limits its use is the availability of autologous serum. To date, autologous serum has been primarily used at academic centers with laboratory facilities to prepare it. At other centers with preparation facilities, there have been some problems with its use because of the lack of regulatory standards and the potential risk of infection if the serum is not prepared, stored, and used in the proper fashion.[15] Ideally, the preparation of autologous serum is best handled by trained blood banking personnel in a standardized fashion under aseptic conditions.[13]
4. Finally, although autologous serum accelerates epithelial healing in patients with persistent epithelial defects, its effect on pain has not been fully validated. Patients with corneal epithelial defects cannot open their eyes because of pain and foreign body sensation, and the addition of a contact lens could resolve this problem. In monocular patients, the application of bandage contact lens helps them open their eyes and function normally. I think that if we could resolve the problems in preparing autologous serum eye drops for such patients, the combination of a bandage contact lens and autologous serum eye drops would be the best way to treat corneal epithelial defects.

It is likely that on resolving such problems in the use of autologous serum, it will become the main therapeutic modality for treating persistent corneal epithelial defects, especially after vitreoretinal surgery.

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Suture-Pull Technique for Insertion of Donor Lenticule in Endothelial Keratoplasty

To the Editor:

We read with interest the suture technique for Descemet stripping and endothelial keratoplasty described by Macsai and Kara-Jose.[1] We would like to share with readers our technique, which we feel has additional advantages compared with that described by the authors. Our initial experience with Descemet stripping automated endothelial keratoplasty using a noncrushing forceps to insert the donor lenticule has been very encouraging, but we, and many others, feel that protecting the endothelium is the cornerstone for long-term good outcome of this new procedure.[2] We insert the donor lenticule using a suture-pull technique through a glide (Moria #19098) that gently folds and introduces the donor lenticule without creasing. This results in easy insertion and immediate unfolding of the lenticule in the anterior chamber, which must be better for the long-term survival of the endothelial cells compared with using a forceps.

We used the technique in 6 eyes, with excellent results as follows. The edge of the donor lenticule is gently grasped with fine double fixation forceps, and an Alcon 10–0 polypropylene looped monofilament suture mounted on a ¼ circle side-cutting needle (PC-9) is passed through the edge of the lenticule (Fig. 1A). The suture is advanced until the loop is approximately 2 cm from the edge of the lenticule, and then the needle is passed through the loop to secure the lenticule at the end of the suture (Fig. 1B). The needle is subsequently passed through the glide nozzle (Fig. 1C), and the lenticule is loaded stromal side down into the glide and pulled into its opening. Next, the needle is passed through the incision into the anterior chamber and out through the peripheral cornea of the recipient. The glide is inverted and positioned into the incision (5 mm), and the suture is simply pulled to introduce the lenticule into the anterior

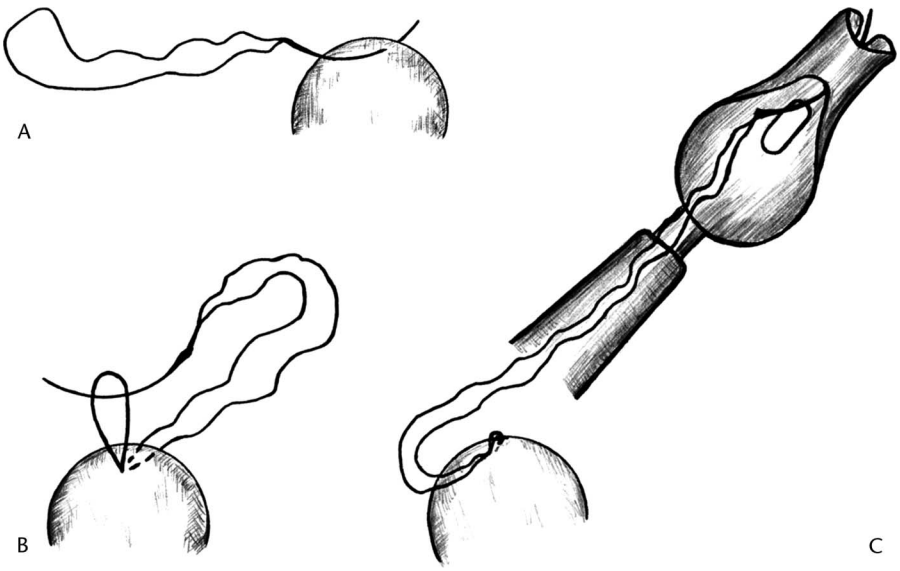

FIGURE 1. A–C, Schematic drawing of the modified suture-pull technique for Descemet stripping automated endothelial keratoplasty.

chamber where it unfolds spontaneously with the help of irrigation from an anterior chamber maintainer. The flow through the anterior chamber maintainer is controlled by the foot pedal of a phacoemulsification machine on irrigation mode with a balanced salt solution bottle 50–60 cm high from the eye. The polypropylene suture loop is then cut and pulled out.

The suture (Alcon #8065307901) was originally designed for fixating intraocular lens implants in the absence of posterior capsule support. It facilitates pulling the donor lenticule using 1 needle pass through the anterior chamber, therefore avoiding potential complications and providing fewer needles to contend with during the procedure. The glide allows gentle folding of the lenticule without the need for forceps, which results in creasing that may damage the endothelial cells at the crushing line. This technique simplifies the whole procedure and should be a great advantage in protecting the endothelium. We are prospectively evaluating the endothelial count after Descemet stripping automated endothelial keratoplasty using this technique and hope to report our results in future.

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Advantages of Suture-Pull Technique for Descemets Stripping and Endothelial Keratoplasty

Reply:

Drs. Habib and Gomaa have submitted a letter describing an alternative insertion technique for Descemet stripping automated endothelial keratoplasty surgery using a suture-pull technique and a Moria glide. They have postulated that the use of the glide without folding the tissue may limit the damage to the endothelium during graft insertion. After insertion using a suture-pull technique, the authors elect to cut and remove the suture once the donor lenticule is centered.

They have introduced the use of the Moria glide to decrease the endothelial damage that results from folding and inserting the tissue. This may be less traumatic to the endothelial cells, and further studies with careful attention to the pre- and postoperative endothelial cell counts will be necessary to validate this statement.

Drs. Habib and Gomaa have discussed the use of a suture to pull the lenticule of endothelial cells into position and cut the suture at the end of the case. Their technique of locking the suture before insertion and then cutting the loop after the tissue is in place may be traumatic to the tissue. Displacement of the lenticule could occur when the suture is removed. It would be easier to simply tie the suture in a single loop and cut the loop to remove the suture.

Removal of the suture will make repositioning of the tissue necessary if adherence is not achieved on the first postoperative visit and the lenticule dislocates into the anterior chamber. In addition, if there is a need to inject additional air or rebubble in the postoperative period, it is difficult to get the air behind the donor lenticule once it is dislocated. In our technique, the surgeon sits at the head of the patient and the suture is passed through the cornea at the 6 o'clock position and left in place for the first postoperative visit. After air is injected into the anterior chamber at the end of the case, the patient is sent home and told to recline but not required to lay supine. In this way, the air bubble travels to the superior half of the anterior chamber, not blocking the pupil, decreasing the risk of pupilary block. The air bubble holds the superior half of the lenticule against the cornea, and the inferior half is held in position with the suture at 6 o'clock. Patients are more comfortable reclining than laying flat. On the first postoperative day, if there is a slight dislocation or separation of the lenticule from the cornea, rebubbling can be performed at the slit lamp under direct visualization. The lenticule is still held in place by the 6 o'clock suture; therefore, a 30-guage needle is introduced at the 6 o'clock limbus and the air is injected posterior to the lenticule. By performing this procedure at the slit lamp, visualization of the position of the needle in the anterior chamber is increased.

Drs. Habib and Gomaa have made additions to this rapidly changing technique of corneal transplantation, which may decrease the trauma to the donor endothelial cells. However, this claim will need to be validated with further studies.

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Deep Lamellar Keratoplasty in Keratoconus With Healed Hydrops

To the Editor:

We read with great interest the article by Das et al[1] on deep anterior keratoplasty in a 17-year-old adolescent boy with presumed healed hydrops. However, there are some important issues that should be addressed.

First, the definite diagnosis of corneal hydrops was not clear. There is no definite report of acute hydrops or any document that support the rupture of Descemet membrane (DM) before surgery in this case. The authors presumed that the patient had acute corneal hydrops due to a central corneal scar that may be seen in patients with keratoconus without corneal hydrops, especially in this case with a history of Rigid Gas Permeable wearing for 3 years and vernal keratoconjunctivitis.

Second, ruptures of DM that cause corneal scarring will never repair completely. The authors used air bubble injection and baring the DM by removing the stroma layer by layer. It is hard to believe that a previously ruptured DM can resist injection of air bubble in deep corneal stroma by an intensive pressure and can be stripped thoroughly intact during surgery.

Third, even if one can perform a pre-Descemet lamellar dissection by air injection in the superficial and midstromal layers, a significant deep stromal scar may remain after surgery (just like what is seen in figure 2 in their case), which may significantly limit the postoperative visual acuity and contrast sensitivity in a young patient.

In conclusion, we think DLK can be performed in selected cases of limited hydrops only in its conventional form or by air injection in the superficial and midstromal layers and performing a pre-Descemet lamellar dissection, provided that the remaining scar is not on the visual axis of the patient and the predicted postoperative visual acuity is acceptable. Injection of the air bubble in deep stromal layers and stripping the DM have a significant risk of rupturing the DM in a patient with the history of corneal hydrops and are not recommended especially in patients with vernal keratoconjunctivitis because penetrating keratoplasty after an intraoperative failed DLK due to DM rupture may be associated with a high risk of graft endothelial rejection in these inflamed eyes.

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Reply:

We thank Jabbarvand and MohammadPour for their interest in our article. We agree that long-standing inflammatory disease and use of rigid gas permeable contact lenses may lead to deep and dense corneal scar due to chronic damage to the Bowman membrane, and the clinical appearance in such a case may be confused with a healed hydrops scar. Patients with acute hydrops typically report acute onset of blurred vision, ocular irritation or pain, watering, and photophobia, and frequently notice corneal opacity that can be visible to unaided eye. Our patient had a similar history in his left eye. In addition, in our patient, a few thick Descemet membrane (DM) folds and linear scars were seen postoperatively under high magnifications (figure 1b of our article), which were suggestive of healed hydrops.

After hydrops, the DM tear heals by migration of the endothelium over the area of rupture in 4–6 months.[1] The endothelium starts laying the new DM. Big bubble technique is certainly contraindicated in cases of healed hydrops scar. As mentioned in our article (in second paragraph of the "Case Report" section of our article), we injected intrastromal air bubble (Archila technique) and the lamellar dissection was done layer by layer.[2]

Despite the presence of residual scar in the DM, our patient had a final best corrected visual acuity of 20/20. Decreased contrast sensitivity is certainly a concern for a young patient. However, it is necessary to weigh the risk–benefit ratio of penetrating keratoplasty (PK) versus deep lamellar keratoplasty (DLK) in terms of younger age of the patients, higher rate of graft rejection, and incidence of graft failure over longer duration in PK as against the assumed diminution of vision due to the remnant scar in the DM in DLK. DLK provides a safer and successful alternative to PK for keratoconus patients but remains a challenging procedure.

We do not feel that failed DLK due to rupture of DM will have higher rate of rejection compared with planned PK cases. We are not aware of any scientific study supporting this concept. We conclude that DLK may be a better option in cases of healed acute hydrops especially where the visual axis is spared.

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Optical Coherence Tomography of Descemet Membrane Separation by the Big Bubble Technique

The article by Kaiserman et al[1] describes an elegant way of imaging the big bubble technique by optical

coherence tomography (OCT), and the authors need to be commended on their innovative use of OCT. There are a few clarifications that I seek from the authors. The depth of the needle on the OCT image appears to be superficial (fig. 1A, B) and not 400 μm as mentioned in the text; also, the initial spread of the air along the stromal lamellae also appears to be in the mid-stromal level at the level of the penetration of the needle.

There are some suggestions for surgeons who attempt this technique during surgery. To enhance the chances of success in achieving the big bubble, anterior lamellar dissection after trephination is helpful; it ensures better visualization of the tip of the needle and deeper penetration in to the posterior stroma. There are 3 signs described[2] to ascertain whether the big bubble has been achieved. First, blanching of the corneal stroma spreads in a wave-like circular fashion with a true bubble. Second, a completed bubble frequently exhibits a feathery white band at its circular periphery. Third, the anterior surface of the cornea "rises" as the bubble takes up some space in the central cornea. However, it is not without surgical challenges, such as visualization and confirmation of the big bubble. The "small bubble" technique of injecting air into the anterior chamber to observe its behavior that has recently been published is an additional tool to confirm that the big bubble has been achieved[3]. I thank the authors for their efforts.

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Optical Coherence Tomography of Descemet Membrane Separation by the Big Bubble Technique

Reply:

I thank Dr. Parthasarathy for his comments and for sharing with us his suggestions on how to succeed in creating the big bubble. Regarding the depth of the needle in our recently published study,[1] we trephinated the cornea at a depth of 400 μm and attempted to insert the needle at the same plane as the trephination. We did not use optical coherence tomography to establish the depth of the needle, and it is possible that in the case depicted in figure 1, the needle might have been more superficial. However, one should keep in mind that in our study, we used human corneas preserved in Optisol-GS for 10–14 days after death. During such a long preservation period, the corneas might swell, reaching a thickness of about 600–800 μm. Thus, a 400-μm trephination would be about half way into the cornea, which is more or less what is depicted in figure 1. Despite the relative shallow depth of air injection, a big bubble was created in all 5 corneas in this study.

In my clinical experience, the initial rate of air injection into the cornea is crucial to the success of creating the big bubble. As reported in our study, once injected into the stroma, air seems to readily spread among the stroma lamellas at the level of penetration of the needle. To force air into the supra-Descemet space, one needs to create sufficient pressure at the tip of the needle to enable air to break through lamellas, rather than to spread laterally along the lamellas. Thus, a rigorous injection of air into the stroma has a better chance of creating the big bubble. I recommend an initial fast buildup of air pressure in the syringe to force the air deep into the stroma before it has managed to escape laterally.

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