New Trends in Antimetabolite Use

The intraoperative injection of mitomycin C.

BY ALBERT S. KHOURI, MD

The use of antimetabolites, particularly mitomycin C (MMC), is standard during glaucoma filtration surgery. In addition to the agent's classic indications (eg, young patients or previous incisional surgery), evidence suggests that the long-term use of topical glaucoma medications induces a chronic inflammatory state that is detrimental to trabeculectomy's success. It has therefore become common practice for surgeons to use MMC intraoperatively almost routinely during trabeculectomy. The technique with which the agent is applied, however, varies.

SPONGE APPLICATION

At present, most surgeons soak sponges made of different materials and sizes (cut pieces of a corneal shield or a Weck-Cel spear [Beaver-Visitec International]) with MMC prepared to different concentrations. A disadvantage of this approach is the surgeon's inability to determine the actual quantity of the drug delivered to the tissues. In one study, it was estimated that the actual dose delivered in a sponge soaked with MMC 0.2 mg/mL varied between 1.9 and 17.3 µg.[1] Moreover, the effect of irrigating the site of MMC application with saline is variable. In an in vitro study, irrigation at the site of MMC sponge application influenced the level of the antifibrotic in the superficial scleral layers but had no effect on the deeper layers, where MMC had already diffused.[2] A third variable is the size of the sponge. Corneal shields come as discs that are 7, 8, or 10 mm in diameter and are then cut in half.

A downside of sponge application is that it can create a whitish MMC "burn." The avascular, thin bleb produced is at increased risk of early and delayed leaks as well as of infection. Such localized filtering blebs tend to be functionally limited by encapsulation and sequestration within what is classically described as a "ring of steel" (ie, surrounding Tenon fibrosis). Also, surgeons must use multiple sponges for a more diffuse application, all of which must be carefully collected thereafter.

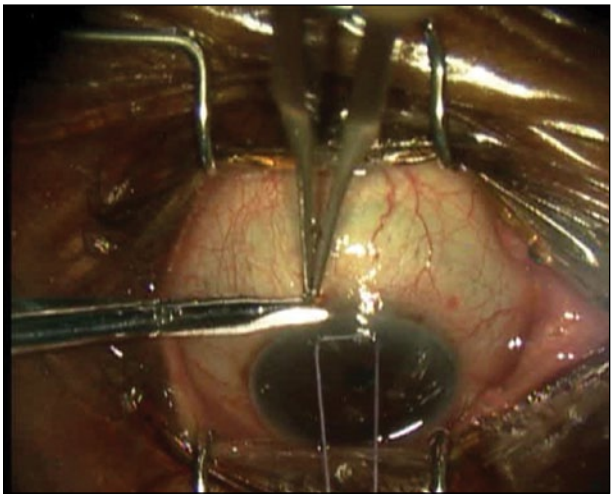

Figure 1. A conjunctival peritomy is initiated with scissors.

WHY INJECT?

Multiple investigators have reported success after injecting MMC during bleb revision.[3,4] By injecting MMC during trabeculectomy, the ophthalmologist can calculate the exact amount of antimetabolite delivered to the surgical site. The technique also ensures consistency: the same dose is delivered every time to every patient. Another advantage to intraoperative injections is a wide area of application from the subconjunctival dissipation of MMC. Multiple sponges would be required for the same coverage.

TECHNIQUE

First, I prepare the injectable MMC. For most cases, I use 10 or 20 µg. For a 20-µg preparation starting with MMC 0.4 mg/mL, I dilute 0.1 mL of MMC (40 µg) in 0.1 mL of lidocaine (1:1, total volume of 0.2 mL). I

TEN YEARS OF THE INTRA-TENON INJECTION OF MITOMYCIN C

By Iqbal Ike K. Ahmed, MD

My colleagues and I have been injecting mitomycin C (MMC) as part of external glaucoma filtering procedures for over 10 years now. We feel this is a more controlled, potentially more effective, and certainly more efficient method of drug delivery. We have used this approach in more than 300 eyes.

INSPIRATION

We began by using adjunctive MMC as part of needling failing filters. Our standard approach has been a pre-needling injection of MMC (0.2 mg/mL, 0.1 mL) within Tenon capsule, 8 mm from the limbus, superior to the bleb. The injection, which forms a subconjunctival elevation, diffuses over an area just posterior to the bleb and is quickly bound by the tissue. We perform needling 10 to 15 minutes later to ensure that there is no free MMC in solution to prevent its entry into the anterior chamber. All of these steps are executed at the slit lamp under topical anesthesia.

Our experience led us to perform an intra-Tenon injection of MMC as part of trabeculectomy surgery versus the more classic sponge application. Our technique is very similar to what we do for office-based needling.

OUR TECHNIQUE

With the patient on the stretcher in the holding area, we perform the intraoperative injection under direct visualization with a speculum in place. Another option would be to use a pair of loupes. Alternatively, if available, the surgeon could perform the injection at the slit lamp in the perioperative area. After topical antibiotics and anesthesia, with the patient looking down, we inject 0.2 mL of MMC using a 30-gauge needle in the adjacent quadrant of the intended trabeculectomy dissection. We use a cotton swab to move the conjunctiva towards the intended quadrant in order to place the needle entry point as far away from the bleb site as possible.

The 30-gauge needle enters approximately 6 mm from the limbus in the adjacent quadrant (Figure 1). We direct the needle towards—but not into—the area of the future bleb and pass it under the conjunctiva for at least 3 mm, while being careful to avoid any vessels. We strongly prefer to avoid a subconjunctival hemorrhage, which we have found to be rare with careful technique. Prior to injection, the needle is 6 to 8 mm from the limbus, under the conjunctiva and just adjacent to the intended bleb location. We inject the MMC and then withdraw the needle along the same tract. A cotton swab is applied at the needle entry to tamponade the microscopic needle incision point, and we use the swab to massage the subconjunctival injection into the adjacent quadrant of interest (Figure 2). Because the needle is not placed directly in the quadrant of intended surgery, potential subconjunctival hemorrhage over the bleb is avoided. By injecting the bolus of MMC, and then massaging it into the area of intended effect, we avoid hemorrhage in the direct filtration path of the bleb if it were to occur. This could affect visibility during surgery, alter the MMC effect, and add a stimulus for inflammation, scarring, and bleb failure.

Figure 1. The surgeon injects MMC into the superior quadrant with a 30-gauge needle.

Figure 2. A cotton swab is used to massage MMC into the superior-nasal quadrant.

The needle tract typically seals on its own. To encourage the antimetabolite effect to create a more posterior and diffuse bleb and to avoid a potential impact at the limbal incision (we use fornix-based flaps), we prefer to see the injection fluid reach within 2 mm of—but not right up to—the limbus. Thus, a second cotton swab

TEN YEARS OF THE INTRA-TENON INJECTION OF MITOMYCIN C *(CONTINUED)*

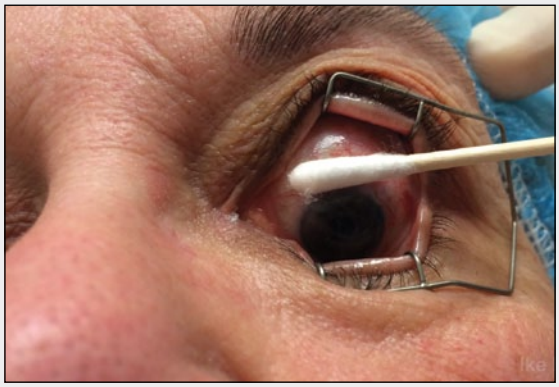

Figure 3. A second cotton swab massages MMC away from the limbal area.

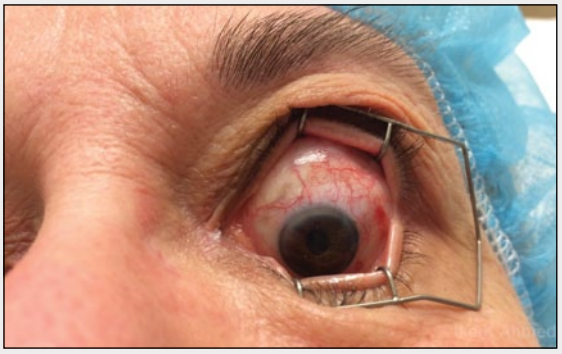

Figure 4. The bleb is visible in the area of intended filtration surgery.

may be placed at the limbus to prevent the MMC injection from reaching the limbus and keep it more posterior (Figure 3). Both cotton swabs can be used to massage the fluid to the optimal location as needed (http://bit.ly/PxOzPA).

OUR RESULTS

Although a decade ago very few surgeons were using this technique, interest has grown. In 10 years, we have not seen an increase in the risk of complications with injection versus sponge delivery of MMC. In fact, our results are quite favorable. Not only is the dose more consistently delivered and titratable compared to the variability with sponge delivery, we find that the application area is more diffuse, which promotes a more diffuse posterior bleb (Figure 4). In fact, our anecdotal experience found less cystic and avascular blebs with injection versus sponge delivery. Finally, we saved OR time by performing the injection preoperatively as opposed to the set time (2-5 minutes) of sponge application intraoperatively. We vary our dosing (0.2 to 0.5 mg of MMC in 0.2 mL) depending on the patient's risk factors for bleb failure. This seems to be a more logical approach to titrating the dosage as opposed to the length of time of sponge application, especially considering that MMC typically reaches tissue saturation by 90 seconds. Some surgeons have combined lidocaine with the MMC injection, but we find it unnecessary.

At the 2013 American Glaucoma Society Annual Meeting, Michele Lim, MD, James Brandt, MD, and colleagues from the University of California, Davis, presented a retrospective comparison to sponge delivery.[1] They found trabeculectomies with MMC injection achieved similar IOPs but less postoperative medication use and less bleb encapsulation. More importantly, MMC injection appeared to be safe. I am aware of at least one randomized controlled trial studying injection versus sponge delivery of MMC for trabeculectomy.

Now, my colleagues and I are injecting MMC as an adjunct to novel microinvasive subconjunctival devices for glaucoma surgery in patients at high risk of failure. Thus far, our results are promising.

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1. Lim M. A comparison of trabeculectomy surgery outcomes with mitomycin-C applied by intra-Tenon injection versus sponge method. Paper presented at: The American Glaucoma Society Annual Meeting; March 2, 2013; San Francisco, CA.

then use half of that solution (ie, 0.1 mL of the MMC-lidocaine [20 µg]) for injection.

After the instillation of topical anesthesia, I perform a small snip incision at the limbus (or elsewhere depending on the type of conjunctival incision; Figure 1). Next, I introduce a blunt 30-gauge cannula 7 to 8 mm from the limbus, where I slowly inject the MMC (Figure 2). I am careful to keep the incision small, because MMC can reflux through the incision to the ocular surface if the original snip incision is generously sized. The conjunctival entry can be compressed with a Weck-Cel spear to prevent any MMC from escaping (Figure 3). The blunt cannula is withdrawn, and the solution can be further spread over a larger surface area using a Weck-Cel spear.

I then complete the conjunctival peritomy. Wet field bipolar cautery can be used for hemostasis, and the

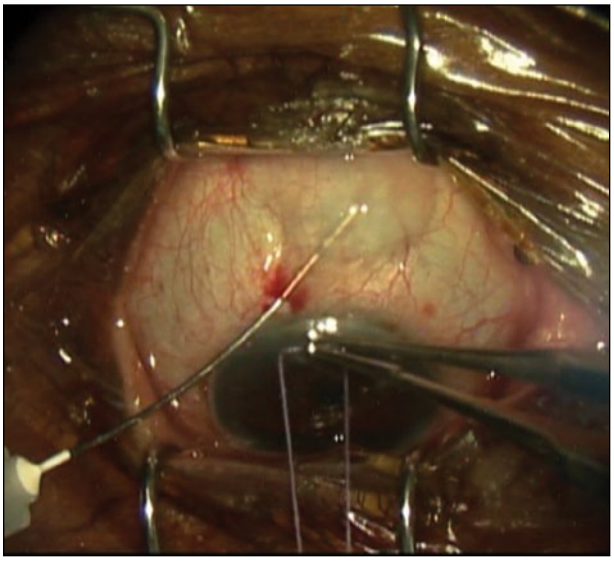

Figure 2. A blunt-tipped cannula is introduced subconjunctivally for the injection of MMC.

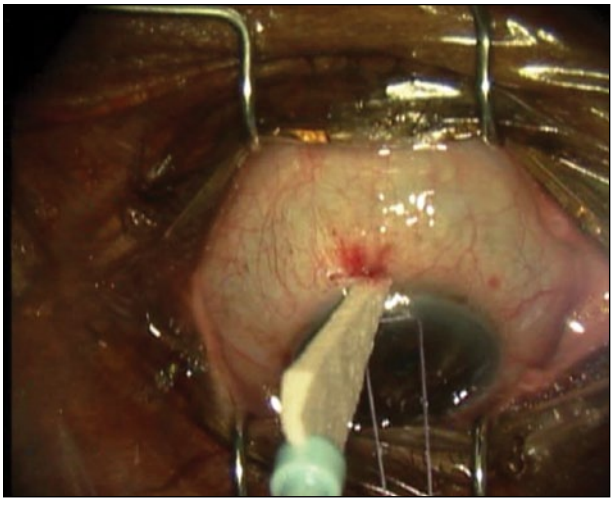

Figure 3. Compression of the conjunctival incision prevents the reflux of MMC to the ocular surface.

surgery is concluded in the usual fashion. I have found the lidocaine to be sufficient for anesthesia in many patients. In others, I will supplement with sub-Tenon lidocaine as needed.

INITIAL EXPERIENCE

The risks of intraoperative MMC use in trabeculectomy are well known, and they can be severe, even vision threatening (eg, corneal decompensation, scleral thinning, hypotony, increased risk of bleb leaks and infection). At Rutgers University, a review of trabeculectomy cases performed with MMC administered via intraoperative injection versus sponge application (N = 50 eyes, 25 eyes in each group) with 6-month follow-up demonstrated similar IOP efficacy and safety profiles (A.S.K., unpublished data, 2014). Although the injection group had a lower mean IOP overall and a higher proportion of its members achieved an IOP reduction of more than 30% from baseline than the sponge group, the difference did not reach statistical significance. Of note, the injection group needed significantly fewer postoperative interventions (5-fluorouracil and laser suture lysis) than did the sponge group.

> "This technique allows surgeons to deliver an accurately predetermined dose of MMC over a larger surface area than is readily achievable with traditional sponge application."

CONCLUSION

The intraoperative injection of MMC during trabeculectomy seems to be safe and effective. This technique allows surgeons to deliver an accurately predetermined dose of MMC over a larger surface area than is readily achievable with traditional sponge application. ■

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