

Cataract

Performing Surgery Without Hyaluronidase

BY JOHN C. HAGAN III, MD

CASE PRESENTATIONS

Case No. 1

A 65-year-old white female had previously undergone an uncomplicated phacoemulsification cataract removal and insertion of an IOL OD. The procedure was performed under topical anesthesia (lidocaine gel and intracameral lidocaine) by another surgeon. The patient complained of severe intraoperative pain, fright at having to watch the procedure, and highly uncomfortable photophobia. In spite of having an UCVA of 20/30 and BCVA of 20/20 in the eye, she was unhappy with her previous surgeon. She wanted her other 20/100 cataractous eye treated “with me asleep” or “with a shot like my dentist gives me.”

Case No. 2

A 76-year-old white male underwent an uncomplicated phacoemulsification and insertion of an IOL OD. Preoperatively, I administered a peribulbar injection (4 mL) of 0.75% bupivacaine and 2% lidocaine without Wydase (hyaluronidase; Wyeth Pharmaceuticals, Collegeville, PA). On the first postoperative day, the patient complained of both vertical and horizontal diplopia. One year earlier, he had undergone a similar procedure without complication. The anesthetic mixture used on the first eye included hyaluronidase.

HOW WOULD YOU PROCEED IN THESE TWO CASES?

1. Would you operate on Case No. 1?
2. Would you perform Case No. 1 under general, injection, or topical anesthesia?
3. If you plan to use injection anesthesia, what additional steps might you take to reduce the patient's anxiety and pain?
4. What is the most likely cause of the patient's double vision in Case No. 2?
5. How would you treat Case No. 2?
6. What can be done to prevent eye muscle complications as described in Case No. 2?

SURGICAL COURSE AND OUTCOMES

Case No. 1

I performed phacoemulsification and IOL insertion on the patient's left eye using a peribulbar injection that included hyaluronidase for anesthetic supplementation. I administered intravenous sedation just prior to the peribulbar injection. She experienced total amnesia from the anesthetic injection. My staff and I gave the patient extra reassurance through “vocal-local,” and the anesthetist held her hand throughout the procedure. The patient was comfortable during and after the procedure and achieved 20/20 UCVA.

Case No. 2

I referred the patient to a strabismus surgeon who followed him for 6 months, but his diplopia failed to resolve. After undergoing strabismus surgery and receiving prism glasses, the patient has single vision in the primary fields of gaze. Without the prism glasses, he has diplopia in all fields of gaze. Adding hyaluronidase compounded by a nationally known pharmacy to the local injection mixture has ended his postoperative diplopia.

DISCUSSION

Hyaluronidase is a spreading enzyme used in various forms of anesthesia since 1949. It is manufactured from bovine testes and depolymerizes interstitial ground substances. This agent speeds the onset, deepens the penetration, and lengthens the duration of injected anesthetics. Hyaluronidase also improves the safety of the anesthetic and surgical procedure.¹ In ophthalmology, surgeons who prefer topical anesthesia often use injection anesthesia with hyaluronidase for difficult patients, while other surgeons perform all of their surgeries with injection anesthesia, ideally using hyaluronidase. Although cataract and anterior segment surgeons are among those who use hyaluronidase most often, retinal surgeons, oculoplastic surgeons, and anesthesiologists also use the product for regional blocks.

In spite of the documented, well-recognized benefits and widespread use of hyaluronidase, Wydase was the only

FDA-approved hyaluronidase product available in the US. Unfortunately, on several occasions, Wyeth Pharmaceuticals experienced production difficulties that caused severe shortages of Wydase. During these hyaluronidase shortages, cataract surgeons noted an increase in postoperative complications, including permanent diplopia and ptosis.¹⁻⁴

In 2000, Wyeth Pharmaceuticals permanently discontinued the production of Wydase. The company ignored pleas from major ophthalmic organizations requesting the reopening of the Wydase production facility. The company profited by the sale of Wydase and has not offered an adequate explanation for abandoning the drug.

The demise of Wydase left the US without an FDA-approved source for hyaluronidase. Efforts by members of the ASCRS and the AAO to induce a domestic or foreign pharmaceutical manufacturer to purchase the production rights to Wydase or repeat another FDA study on hyaluronidase failed. Further, cases of "Mad Cow" disease complicated attempts to import hyaluronidase from Europe.

In response to the needs of surgeons and patients, several pharmacies began compounding a substitute for Wydase from domestic substrate hyaluronidase. One such compounding facility is O'Brien Pharmacy (Kansas City, MO), which has a 40-year-old national reputation for technical excellence. The firm meets or exceeds all industry and state guidelines, including those of the United States Pharmacopeia, American Society of Hospital Pharmacists, National Association of Boards of Pharmacy Good Compounding Practices, and the Missouri Board of Pharmacy. O'Brien Pharmacy compounds products that require ultra-meticulous formulation such as intrathecal medications. At the request of ophthalmologists in Kansas City, the pharmacy prepared a sterile hyaluronidase from US-produced bovine substrate. The product was tested for sterility and potency by outside reference laboratories, and it costs approximately 30% less than Wydase.

Warren Hill, MD, of Mesa, Arizona, and I completed a prospective study⁵ of O'Brien Pharmacy's hyaluronidase compared with Wydase. We ended the study upon exhausting all available supplies of the latter drug. Our study identified O'Brien Pharmacy's hyaluronidase as superior to Wydase (Table 1). Patients reported less intraoperative and postoperative pain with the compounded form of the drug. Moreover, the compound was not associated with infections or abnormal tissue or drug reactions. Subjectively, Dr. Hill and I find the compounded hyaluronidase superior to Wydase, as do anesthesiologists who perform regional blocks at Dr. Hill's ASC.

Because this compounded hyaluronidase is not FDA approved, it is subject to rules, regulations, procedures, and availability that differ both between states and among hospitals and ASCs within the same city and state. Nevertheless,

TABLE 1. WHICH IS BETTER: WYDASE OR O'BRIEN HYALURONIDASE?

WYDASE	O'BRIEN
• Age 73.6	• Age 74.6
• 0 injection complications	• 0 injection complication
• 0 operative complications	• 1 operative complication
• 6 operative pain (12%)	• 0 operative pain (0%)
• 2 required IV medications	• 0 required IV medications
• 3.3 pain score	• 0 pain score
• 24 patients had postoperative pain (48%)	• 6 patients had postoperative pain (12%)
• 2.79 pain score	• 1.83 pain score
• No postoperative complications	• No postoperative complications

thousands of doses of the compound have been used without reported problems, and the O'Brien Pharmacy continues to ship the product to ophthalmologists in many states.

Although the compounded hyaluronidase has been a satisfactory substitute for Wydase, using it involves increased documentation, special informed consents, and additional burdensome costs and handling procedures. The system by which the FDA approves new drugs and devices desperately needs review and reform. The absence of FDA approval for a new source of hyaluronidase, as well as the lack of approval for simple and obviously helpful devices such as the capsular tension ring, are cases of *res ipsa loquitur* (the thing speaks for itself!). ■

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The author would like to note that neither he nor Dr. Hill has a financial interest in O'Brien Pharmacy, and they conducted their study by purchasing the hyaluronidase at its full retail price. O'Brien Pharmacy may be reached at 4321 Washington, Suite 2020, Kansas City, MO 64111; (816) 531-6763 and (800) 627-4360. The owner and compounding Pharmacist is Eric Everett, RPh.

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