Survey of Intravitreal Injection Techniques Among Retinal Specialists in the United States

AMY E. GREEN-SIMMS, NOHA S. EKDAWI, AND SOPHIE J. BAKRI

• PURPOSE: To describe the intravitreal injection technique practice patterns of retinal specialists in the United States from April 8, 2010 to April 21, 2010.
• DESIGN: Questionnaire survey.
• METHODS: All members of the American Academy of Ophthalmology who self-categorized as "Retinal/Vitreous Surgery" were contacted by e-mail to complete an anonymous, 20-question, internet-based survey.
• RESULTS: A total of 765 retinal specialists (44%) responded to the survey. Most respondents wear gloves (58%) and use an eyelid speculum (92%) when performing an intravitreal injection. More than 99% use povidone-iodine preinjection. The majority measure the injection site from the limbus (56%) and inject straight into the vitreous cavity (96%). Most do not displace the conjunctiva (83%). Seventy-two percent routinely assess postinjection optic nerve perfusion, primarily by gross visual acuity measurement (32%). While nearly one third of participants use prophylactic topical antibiotics preinjection, more than two thirds use topical antibiotics postinjection. Forty-six percent perform bilateral simultaneous intravitreal injections. The majority of respondents use a 30-gauge needle for the injection of ranibizumab (78%) and bevacizumab (60%). However, respondents use both a 27- and 30-gauge needle for the injection of triamcinolone acetonide.
• CONCLUSIONS: Retinal specialists in the United States participate in a range of techniques for the care before, during, and after intravitreal injections. Further study is needed to elucidate best practice patterns. (Am J Ophthalmol 2011;151:329–332. © 2011 by Elsevier Inc. All rights reserved.)

DESPITE THE WIDESPREAD ACCEPTANCE OF INTRAvitreal injections for the treatment of a variety of ocular diseases, there is no current consensus upon injection technique or preinjection or postinjection care. Serious adverse effects of intravitreal injection include endophthalmitis, retinal detachment, ocular hypertension, and cataract.[1–5] With the increasing occurrence of patients receiving bilateral simultaneous injections, there remains a need to evaluate best practice pattern techniques to increase patient safety.[6] There have been reports summarizing the risks of intravitreal injections[1] and describing guidelines based on current best evidence and practice.[7–12] However, few elements regarding intravitreal injection technique or peri-injection care stem from evidence-based medicine. This study aims to describe the intravitreal injection practice patterns of retinal specialists in the United States from April 8, 2010 to April 21, 2010.

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From the Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota.
Inquiries to Sophie J. Bakri, Department of Ophthalmology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905; e-mail: bakri.sophie@mayo.edu

METHODS

ALL MEMBERS OF THE AMERICAN ACADEMY OF OPHTHALmology (AAO) who self-categorized as "Retina/Vitreous Surgery" were contacted by e-mail to complete an anonymous, 20-question, internet-based survey. In March 2010, there were 2058 AAO members who self-categorized as "Retina/Vitreous Surgery." Among those physicians, 253 did not list an e-mail address. Seventeen e-mail addresses were recorded for more than 1 physician. Therefore, 1788 surveys were e-mailed on April 8, 2010. Sixty-eight e-mails were returned to sender as the addresses were no longer valid. This study, therefore, included 1720 total survey participants. Three reminder e-mails were sent to participants who had not yet completed the survey. Study data were collected and managed using REDCap electronic data capture tools hosted at the Mayo Clinic. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation; and 3) automated export procedures for seamless data downloads to common statistical packages. Results were tabulated on April 21, 2010.

RESULTS

BY APRIL 21, 2010, 765 OF 1720 RETINAL SPECIALISTS (44%) responded to the survey. Among participants, 279 (37%) worked in a retina-only group practice, 225 (29%) worked in a multispecialty group practice, 126 (16%) worked in a solo practice, 109 (14%) worked in a university setting, 19 (2%) worked in a combination of the above settings, and 6 (1%) described their setting as "other." The participants

were nearly evenly divided in terms of length of time practicing, after the completion of a retina/vitreous fellowship. Twenty-four percent (180/761) have practiced between 1 and 7 years post-fellowship, 26% (196/761) have practiced between 8 and 15 years post-fellowship, 28% (216/761) have practiced between 16 and 25 years post-fellowship, and 22% (169/761) have practiced for over 25 years since fellowship completion. Sixty-seven percent of respondents (513/762) performed 10 to 50 intravitreal injections per week. Eighteen percent (138/762) performed 0 to 10 injections per week, and 15% (111/762) performed >50 injections per week.

- **PREINJECTION CONSIDERATIONS:** Fifty-eight percent (439/762) of respondents don gloves to perform an intravitreal injection. Among those who wear gloves, 58% (254/439) wear sterile gloves and 42% (185/439) wear clean gloves. The majority of respondents do not use a sterile drape (88%; 668/759), yet do use an eyelid speculum (92%; 700/760). Nearly all respondents use povidone-iodine preinjection (758/761). One third of retinal specialists use prophylactic topical antibiotics either for a multiday course preinjection or immediately prior to an injection (34%; 257/758).

- **INJECTION TECHNIQUE:** Approximately half of the survey respondents (56%; 424/762) measure the distance from the limbus to the injection site. Among those who measure, 66% use calipers (280/424), 28% use a tuberculin syringe (119/424), and 6% use another device (25/424). Few respondents displace the conjunctiva prior to injection (17%; 129/761) or tunnel the needle during injection (4%; 33/758). Among the 59% of participants (448/757) who consider the speed of the jet of fluid they inject, a majority (76%; 340/448) inject quickly. A majority of survey participants use a 30-gauge needle for the intravitreal injection of ranibizumab (Lucentis; Genentech, South San Francisco, California; USA) and bevacizumab (Avastin; Genentech) (78%; 581/745 and 60%; 455/759 respectively). Most respondents use a 27-gauge needle for the intravitreal injection of triamcinolone acetonide (Kenalog) (57%; 418/738). A similar amount of retinal specialists use a 27-gauge vs a 30-gauge needle for the injection of triamcinolone acetonide (Triesence) (43%; 301/697 and 44%; 310/697 respectively).

- **POSTINJECTION CONSIDERATIONS:** Nearly three quarters of the survey respondents routinely assess postinjection optic nerve perfusion (72%; 546/759). Among those who assess optic nerve perfusion, 32% (176/546) perform a gross visual acuity examination (finger count or hand motion assessment), 21% (116/546) visualize the optic nerve, 15% (83/546) measure the intraocular pressure, and 31% (171/546) use a combination of the above techniques. A majority of retinal specialists (81%; 608/753) use prophylactic topical antibiotics postinjection. Nearly half of the survey respondents (46%; 348/763) perform bilateral simultaneous intravitreal injections.

DISCUSSION

THE INTRAVITREAL INJECTION OF MEDICATION HAS gained tremendous acceptance among retinal specialists for the treatment of a number of conditions including age-related macular degeneration, diabetic retinopathy, and macular edema. Variations, however, remain on injection technique and preinjection and postinjection care. We report upon a survey of techniques employed by retinal specialists across the United States from April 8, 2010 to April 21, 2010.

- **PREINJECTION CONSIDERATIONS:** This study finds that one third of survey participants (33%; 254/762) wear sterile gloves for intravitreal injections. In comparison, 90% of medical retina specialists and 85% of vitreoretinal specialists surveyed in the United Kingdom in 2004 reported wearing sterile gloves.[10] Bhavsar and associates recently reported a low rate of endophthalmitis among patients enrolled in the Diabetic Retinopathy Clinical Research Network Laser-Ranibizumab-Triamcinolone (DRCR Network LRT) clinical trials, whereupon the study protocol did not mandate sterile gloves.[13] Since the syringe containing the drug may not be sterile, it is therefore not necessary to use sterile gloves, as long as the tip of any instrument touching the eye remains sterile.

  Preinjection treatment with topical antibiotics was used by approximately one third of survey respondents. Moss and associates recently reported that the frequency of conjunctival bacterial growth was similar with a preinjection povidone-iodine cleaning either with or without a 3-day course of topical antibiotic.[14] With the increasing frequency of injections given per patient per year, physicians should be aware of the risk of inducing antibiotic resistance. In addition, despite preinjection antibiotics and povidone-iodine preparation, studies have reported rare bacterial contamination of intravitreal injection needle points.[15,16]

- **INJECTION TECHNIQUE:** In order to measure the site of the injection from the limbus, 66% of study respondents used calipers, 28% used a tuberculin syringe, and 6% used another method. Nearly half (44%) of participants, however, used no method of measurement to ensure an injection through the pars plana. Large study protocols have specified that intravitreal injections are to be made in the inferotemporal quadrant 3.5 to 4 mm from the limbus.[17] There remains an increased risk of retinal detachment with a more posterior approach and an increased risk of traumatic cataract formation with a more anterior approach. There is also a risk of hemorrhage if the needle penetrates the ciliary body.

Most survey respondents (83%) did not displace the conjunctiva prior to injection. There have been several studies, however, examining the construction of wound entry for maximal vitreal retention of medication. Rodrigues and associates reported that a tunneled scleral incision, performed by inserting the needle in a 30-degree angle parallel to the limbus with a subsequent perpendicular repositioning halfway during scleral insertion, resulted in significantly less subconjunctival reflux of medication as measured by width of the postinjection subconjunctival bleb.[18] In their study, however, needle gauge was not reported. Upward mobilization of the conjunctiva was performed before the straight injection technique; no mention of conjunctival manipulation was reported before tunneled incisions. Lopez-Guajardo and associates similarly reported a significant reduction in intravitreal drug loss after an oblique injection technique.[19] After grasping limbal conjunctiva to stabilize the globe, a 27-gauge needle was inserted at a 30- to 40-degree angle to the scleral plane and aimed equatorially towards the six-o'clock position. Thirty minutes after injection, a significantly smaller subconjunctival bleb as measured by ultrasound biomicroscopy was found in eyes that were injected at an oblique angle vs a straight injection. Other techniques to reduce drug reflux include holding a sterile cotton-tipped applicator over the injection site for a period of seconds.

A majority of participants in this study reported using a 30-gauge needle for the intravitreal injection of both ranibizumab and bevacizumab. There was less of a consensus among retinal specialists, however, in the injection technique of triamcinolone acetonide. Both 27-gauge and 30-gauge needles were used with frequency for the injection of Kenalog and Triesence. The use of a larger-diameter needle likely relates to steroid drug preparation in which particles may clog a finer needle. Our survey did not specifically poll retinal specialists regarding needle choice for medications prepared by compounding pharmacies. Chen and associates report that vitreous prolapse was observed after intravitreal injection with both 27- and 30-gauge needles.[20] Furthermore, Pulido and associates report that 27-gauge needles require almost twice the force to penetrate the sclera as 30- or 31-gauge needles, which require a similar force for scleral penetration.[21] This has implications for patient comfort during intravitreal injections; a 31-gauge needle may induce less pain.[22]

Our survey reports that a majority of retinal specialists consider the speed with which they inject medication into the vitreous cavity. Among those who consciously manipulate the syringe plunger, most inject quickly. In Aiello and associates' guidelines for intravitreal injection, they recommend a "moderately slow injection" to reduce excessive drug dispersion in the vitreous cavity and to prevent the needle from displacing off of the syringe.[7] Peyman and associates report using a slow technique to "avoid jet formation or cavitary flow."[23] In addition, there is a theoretical risk of causing a retinal break with a fast injection of fluid (especially through a larger-bore needle).

• **POSTINJECTION CONSIDERATIONS:** Nearly three quarters of survey respondents routinely assessed optic nerve perfusion after intravitreal injection. We did not specifically survey if retinal specialists alter their practice based on volume of fluid injected. Several reports have characterized a short-term increase in intraocular pressure (IOP) after intravitreal injection, with pressures returning to baseline after a maximum of 30 minutes.[24–28] These studies were performed using straight injection techniques. Knecht and associates compared changes in IOP with straight and tunneled intravitreal injections.[29] They reported no significant difference in IOP 5 minutes postinjection, even though the tunneled injection sites had significantly less vitreal reflux. Aiello and associates recommend monitoring IOP and checking for perfusion of the optic nerve postinjection to assess for ischemic optic nerve damage.[7] It should also be noted that reports exist of persistent intraocular pressure elevation following even a single injection of ranibizumab[30] or triamcinolone acetonide.[31]

While a majority of respondents in this study did not use prophylactic topical antibiotics preinjection, 81% used topical antibiotics postinjection. A recent analysis of the participants of the DRCR Network LRT trials, where topical antibiotic use was not part of the protocol for intravitreal injections, reported a low rate of endophthalmitis.[13] However, reports of the development of endophthalmitis do remain.[32,33] Topical antibiotics should be used no more than 3 days postinjection to limit drug resistance in the community.[7]

Limitations of this study include a survey response rate of 44%. Bias may be introduced depending on the participants who chose to reply. Despite our limitations, we are able to report current practice variations in the United States regarding intravitreal injection techniques among retinal specialists.

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