

Update on Endophthalmitis After Anti-VEGF Injection

Standardized preparation may be a factor in low infection rate.

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In 2005, with the approval of the first pharmacologic agent for inhibition of vascular endothelial growth factor (VEGF) to treat neovascularization secondary to age-related macular degeneration (AMD), the anti-VEGF era in ophthalmology began. This era has been marked by the rapid adoption of pharmacologic therapy for neovascular AMD by physicians. Intravitreal injections are given on a frequent basis, often as frequently as monthly. The primary indication for anti-VEGF therapy is for treatment of neovascular AMD, but anti-VEGF injections are also given for other conditions, including central and branch retinal vein occlusions, diabetic macular edema, proliferative diabetic retinopathy, cystoid macular edema, and neovascular glaucoma. Figure 1 shows the increase in the number of anti-VEGF intravitreal injections given at Bascom Palmer Eye Institute's clinics over 4 years.

With these increases in patient volume and number of injections has come increased concern about potential

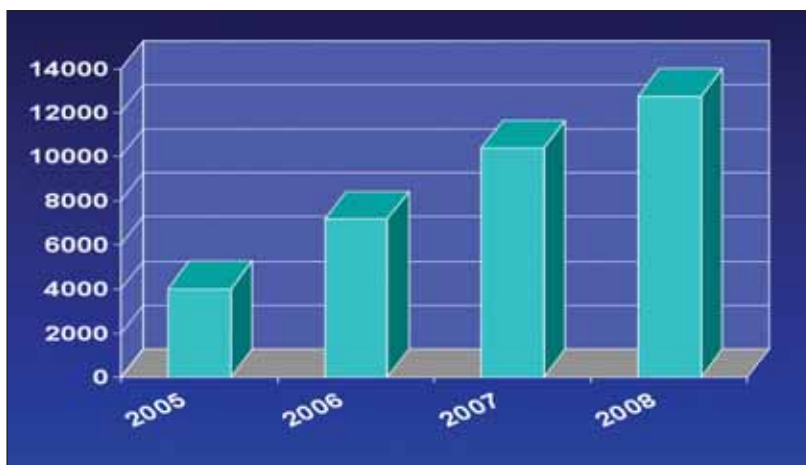


Figure 1. The increase in the number of anti-VEGF injections at BPEI over 4 years.

complications. Rare complications of intravitreal injections include iatrogenic cataract and retinal detachment. More common, although still rare, is the potentially devastating possibility of intraocular infection, or endophthalmitis.

In order to guard against this much-feared complication, it is helpful to have useful information about its incidence. Therefore, we undertook a retrospective study of the incidence of endophthalmitis after intravitreal

anti-VEGF injection at the Bascom Palmer Eye Institute. A full report will be forthcoming in the peer reviewed literature, but preliminary results of the study were presented recently at the Angiogenesis 2010 meeting.¹ This article summarizes some of the information presented there.

LOW RATES OF INFECTION

The purpose of the study was to determine the safety of intravitreal anti-VEGF injections: specifically, to identify the rate of culture-proven endophthalmitis after intravitreal anti-VEGF injections, and to characterize the cases of treated endophthalmitis encountered during this period.

The anti-VEGF era was defined as the period beginning in 2005 with the regulatory approval of pegaptanib sodium.² That approval was followed by reports of off-label use of bevacizumab for treatment of wet AMD,³ and then by the regulatory approval of ranibizumab.^{4,5}

Our study reviewed data from January 1, 2005, through December 31, 2008. To determine the rate of infection, the denominator we used was all intravitreal anti-VEGF injections performed at the Bascom Palmer Eye Institute by Bascom Palmer retina specialists during that period. The numerator was all cases of clinically suspected endophthalmitis: that is, any case that the physician treated as endophthalmitis, not necessarily culture-positive cases. Standard management for endophthalmitis was intravitreal injection of antibiotics or pars plana vitrectomy with intravitreal injection of antibiotics.

During the period under study, 34,278 intravitreal anti-VEGF injections were administered at the four Bascom Palmer Eye Institute sites. Nine cases of clinically suspected and treated endophthalmitis were identified. Five were culture positive on vitreous tap, and four were culture negative. The rate of suspected and treated endophthalmitis among 34,278 total cases was therefore 0.026%, and the rate of culture-positive cases was 0.015%.

Of the nine cases of clinically suspected endophthalmitis, five eyes (56%) had been treated with bevacizumab ($5/22,030 = 0.023\%$), four (44%) with ranibizumab ($4/10,329 = 0.038\%$), and none with pegaptanib.

Two cases (0.009%) were culture-positive after bevacizumab injection, and three (0.03%) after ranibizumab injection (Figure 2).

ACHIEVING A LOW INFECTION RATE

With minor exceptions, the preparation and antibiotic prophylaxis protocols for intravitreal anti-VEGF injections at Bascom Palmer Eye Institute are standardized among all physicians. This standardization may be one factor that has helped us to achieve a low rate of infection after anti-VEGF injection.

No preinjection antibiotic prophylaxis is given: that is,



Figure 2. Representative slit-lamp photograph of a patient with endophthalmitis 1 day following an intravitreal anti-VEGF injection.

antibiotics are not started in the days before the patient's clinic visit.

The preparation is performed by registered nurses in dedicated injection rooms to facilitate patient flow. An eyelid speculum is affixed. The prep technique includes application of 5% povidone-iodine on the conjunctival surface; periocular application of povidone-iodine swab to the eyelids, lashes and adnexa; and topical application of cotton swabs soaked with 4% lidocaine. The cotton swabs are pressed against the sclera in the area of the anticipated injection site, both to soften the eye and to administer the anesthetic. After that, a drop of 5% povidone-iodine is placed on the injection site. This swab-betadine cycle is repeated three times. After the third time, the physician, wearing clean but nonsterile gloves, administers the injection. At the conclusion, typically a drop of antibiotic is placed on the eye, and the eyelid speculum is removed. Intraocular pressure is checked at the conclusion of the injection. Anterior chamber paracenteses are not performed.

Use of postoperative antibiotics varies among physicians at our center. For a large portion of the period of time described in our study, patients were prescribed a topical antibiotic four times daily for 3 days following the injection. Over the past 2 years, a large proportion of Bascom Palmer physicians have opted not to use postoperative antibiotics. (I am among the minority who still prescribe postoperative antibiotics.) It is notable that the Diabetic Retinopathy Clinical Research Network, in recent clinical trials involving the use of anti-VEGF agents,⁶ has not made it mandatory to use postoperative antibiotics.

DISCUSSION AND CONCLUSIONS

The rates of infection in our series of more than 34,000 anti-VEGF intravitreal injections were very low (0.03%) and are comparable with rates reported in other series of anti-VEGF intravitreal injections similar

to ours,⁶⁻⁹ and in the phase 3 clinical trials of pegaptanib¹ and ranibizumab.^{3,4}

Streptococcal species were the most common infectious agents identified in our series and were associated with poorer outcomes than the one staphylococcal infection.

No significant differences were seen between the rates of infection with the anti-VEGF agents included, except that there were no infections in the relatively small number of cases in which pegaptanib was given. The data do not suggest an additional level of risk because of the extra steps involved in the pharmacy preparation of bevacizumab; in fact, the percentage of infections was lower with bevacizumab than ranibizumab, although not statistically significantly so.

One potential strength of this series compared with other large series using pooled data from multiple centers is that, with minor exceptions, the preparation and antibiotic prophylaxis techniques at our center are standardized. With pooled data, it can be difficult to tease out the techniques behind the numbers. The greater homogeneity of our data may make our results easier to interpret. ■

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