Risk of Endophthalmitis After Intravitreal Drug Injection When Topical Antibiotics Are Not Required

The Diabetic Retinopathy Clinical Research Network Laser-Ranibizumab-Triamcinolone Clinical Trials

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Objective: To report the incidence of endophthalmitis after intravitreal drug injection by means of a standardized procedure that does not require topical antibiotics, sterile gloves, or a sterile drape.

Methods: Intravitreal injections of preservative-free triamcinolone acetonide or ranibizumab were administered in 2 prospective randomized clinical trials performed by the Diabetic Retinopathy Clinical Research Network. The standardized procedure for these trials requires the use of a topical combination product of povidone-iodine, a sterile lid speculum, and topical anesthetic, but does not require the use of topical antibiotics before, on the day of, or after injection.

Results: As of February 23, 2009, a total of 3226 intravitreal injections of ranibizumab and 612 injections of preservative-free triamcinolone had been administered. Topical antibiotics were given on the day of injection in 361 (9.4%) of the 3838 cases, for several days after injection in 813 cases (21.2%), on the day of injection and after injection in 1388 cases (36.2%), and neither on the day of injection nor after injection in 1276 cases (33.3%). Three cases of culture-positive endophthalmitis occurred after ranibizumab injections (0.09%), and no cases occurred after triamcinolone injections. In all 3 cases of endophthalmitis, topical antibiotics were given for several days after the injection but not before injection.

Conclusions: The results suggest that a low rate of endophthalmitis can be achieved by means of a protocol that includes use of topical povidone-iodine, a sterile lid speculum, and topical anesthetic, but does not require topical antibiotics, sterile gloves, or a sterile drape.

Trial Registration: clinicaltrials.gov Identifiers: NCT00444600 and NCT00445003

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INTRAVITREAL INJECTIONS HAVE become an increasingly common route of administration of medications in the treatment of posterior segment disease. Endophthalmitis is one of the most serious complications of intravitreal injection of medication, with a reported per-injection incidence that ranges from 0.02% to 1.9%.1-5 Optimum management of the ocular surface before, during, and after intravitreal injections remains controversial.3,6 A topical combination of povidone-iodine is the only preoperative substance proven in a randomized clinical trial to reduce the risk of endophthalmitis after intraocular surgery.7 To our knowledge, no adequate studies have evaluated the role of topical antibiotics; thus, uncertainty still exists with regard to the efficacy of topical antibiotics in the prevention of postinjection endophthalmitis. Although combined use of topical povidone-iodine and antibiotics may have a synergistic effect in reduction of the preoperative culture-positive rate of the conjunctival surface,8-9 we have identified little evidence that suggests topical antibiotics reduce the rate of endophthalmitis in humans. In addition, there is little evidence that the pharmacokinetics of the topical regimens provided would result in adequate antibiotic levels, which would be expected to have a protective effect.10,11 Despite this, topical antibiotics before intravitreal drug injection have been required in several recent clinical trial protocols.14-16 Furthermore, recent surveys have suggested that 40% of retina specialists use topical antibiotics before anti–vascular endothelial growth factor intravitreal injections, and 86% use topical antibiotics after anti–vascular endothelial growth factor intravitreal injections.17,18

Previous studies19,20 have indicated a low rate of endophthalmitis after preservative-free intravitreal triamcinolone acetonide injections in patients for whom pro-
longed topical antibiotic use for multiple days before the injection was not required, ie, for whom antibiotics were required only the day of and the day after the injection. We report the endophthalmitis rate in the Diabetic Retinopathy Clinical Research (DRCR) Network laser-photocoagulation trials in which topical antibiotics administered before or on the day of injection and used for several days afterward were not required but could be administered at the discretion of the investigator.

**METHODS**

The ongoing DCRN Network LRT trials use a standardized protocol for ocular surface preparation and intravitreal injection of ranibizumab or preservative-free triamcinolone. Topical antibiotics may be administered before or on the day of injection at the discretion of the investigator, although neither these nor sterile gloves nor a sterile drape is required. A drop of topical anesthetic is applied to the eye. Two or 3 drops of 5% povidone-iodine may be placed in the lower fornix. The use of povidone-iodine lid scrubs is also optional. Although the use of additional topical anesthetic via cotton-tipped applicators is optional, subconjunctival anesthetic and lidocaine gel or other viscous anesthetic is not permitted, per the protocol. A cotton-tipped applicator soaked in 5% or 10% povidone-iodine is placed directly over the intended injection site or, alternatively, a 5% povidone-iodine–forced stream flush from an angiocatheter is used. In all cases, a sterile lid speculum is used to stabilize the lids. Preservative-free triamcinolone or ranibizumab is injected through the pars plana. Although it is not required, topical antibiotics may be provided and used for several days after injection, at the discretion of the investigator.

Diagnosis of endophthalmitis was given on the basis of the judgment of the investigator, and a culture was required before or on the day of injection received June 24, 2009; accepted June 29, 2009.

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Role of the Sponsor: The funding organization participated in oversight of the conduct of the study and review of the manuscript but not directly in the design of the study, the conduct of the study, data collection, data management, data analysis, interpretation of the data, or preparation of the manuscript.

REFERENCES