lead to tears. Furthermore, it is well established that fellow eyes of patients with RPE tears have a poor visual prognosis and clinicians should be vigilant of future progression in these fellow eyes. Unfortunately, both cases presented were monocular patients with poor fellow eye acuities. Further studies are needed to evaluate histopathological changes which occur after antiangiogenic therapies and whether specific characteristics predispose the development of RPE tears after selective anti-VEGF therapy.

REFERENCES


Absence of Histologic Retinal Toxicity of Intravitreal Bevacizumab in a Rabbit Model

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PURPOSE: To evaluate the retinal toxicity of intravitreal bevacizumab in an animal model.

DESIGN: Animal study.

METHODS: Bevacizumab was injected into the vitreous of one eye of each of eight Dutch-belted rabbits; the other eye served as a control. Four rabbits received a dose of 1.25 mg/0.05 ml of bevacizumab intravitreally into one eye, and the other four rabbits were injected with 2.5 mg/0.1 ml of bevacizumab intravitreally into one eye. At one month, the rabbits were killed and both eyes enucleated. The eyes were fixed with paraformaldehyde 2% and examined by light microscopy.

RESULTS: In all injected and control eyes, there was mild vacuolization in the ganglion cell layer, and disruption of photoreceptor outer segments in both treated and control eyes, to the same degree, consistent with autolysis. The optic nerve, retina, and retinal pigment epithelium were otherwise normal by light microscopy with no evidence of toxicity.

CONCLUSIONS: Intravitreal bevacizumab at doses of 1.25 mg and 2.5 mg showed no signs of retinal or optic nerve toxicity by light microscopy in this rabbit model. (Am J Ophthalmol 2006;142:162–164. © 2006 by Elsevier Inc. All rights reserved.)

BEVACIZUMAB (AVASTIN, GENENTECH INC, SAN FRANCISCO, California, USA) is a recombinant humanized monoclonal IgG1 antibody that inhibits human vascular endothelial growth factor (VEGF). The drug is approved by the Food and Drug Administration for intravenous use in combination with 5-fluoracil based chemotherapy for metastatic colorectal cancer. It has been administered off-label, intravitreally in VEGF-mediated diseases such as choroidal neovascularization,1,2 central retinal vein occlusion,3 proliferative diabetic retinopathy,4,5 and pseudophakic cystoid macular edema.6 Although there are no long-term safety studies in humans, animal studies in albino rabbits have recently shown normal visual evoked potentials and electoretinograms in albino rabbits after intravitreal bevacizumab.7,8 The purpose of this study was to describe the histologic changes after intravitreal bevacizumab in a pigmented rabbit.

Approval was obtained from the Institutional Animal Care and Use Committee at the Mayo Clinic, and the procedures adhered to the guidelines from the Association for Research in Vision and Ophthalmology for animal use in research. Eight Dutch-belted male rabbits (16 eyes) weighing 1.7 to 2 kg (Harlan Laboratories, Indianapolis, Indiana, USA) were anesthetized with 35 mg/kg of intramuscular ketamine hydrochloride (Fort Dodge, Inc, Fort Dodge, Indiana, USA), 5 mg/kg of intramuscular xylazine hydrochloride (Phoenix Scientific Inc, St Joseph, Missouri, USA), and proparacaine hydrochloride 1% ophthalmic drops (Allergan America, Horkiugueros, Puerto Rico) topically on the eye. Povidone iodine 5% was placed on the conjunctiva of eight right eyes. These right eyes were injected intravitreally 3 mm behind the surgical limbus in the superotemporal quadrant with bevacizumab, with four receiving 1.25 mg (0.05 ml), and four receiving 2.50 mg (0.1 ml) of the drug. The eight left eyes were controls and
received no intravitreal injections. Eyes were monitored weekly for signs of inflammation. At 29 days, the rabbits were killed by intravenous pentobarbital overdose (Bue-thanasia-D Special; Schering-Plough Animal Health Corp, Kenilworth, New Jersey, USA). The eyes were immediately enucleated, fixed with paraformaldehyde 2%, paraffin-embedded, and sectioned for light microscopy. The slides were reviewed by two masked and independent observers, an ophthalmic pathologist, and a veterinary pathologist, on two separate occasions, in a random order.

By light microscopy the inner retinal layers in all eyes were intact with no evidence of cellular atrophy or disorganization (Figures 1, 2, and 3). There was mild vacuolization in the ganglion cell layer and disruption of photoreceptor outer segments in both treated and control eyes, to the same degree, consistent with autolysis and tissue processing artifacts. There was no histologic evidence of toxicity to the retina or optic nerve in any of the sections examined. There was no evidence of ocular inflammation or cataract in any of the sections examined.

Bevacizumab is commercially available as a colorless solution, at a concentration of 25 mg/ml. Doses of 1.25 mg (0.05 ml) and 2.50 mg (0.1 ml) were tested, as injecting a greater volume than 0.1 ml into the vitreous may cause a severe acute elevation in intraocular pressure. Although the optimum dose for each disease process remains to be established, previous published reports on intravitreal bevacizumab have used doses of 1.25 mg. The volume of the human vitreous is approximately 4 ml, and the volume of the vitreous in a Dutch-belted rabbit is approximately 1.5 ml. Therefore, a certain amount of drug injected into a rabbit eye is equivalent to a concentration of 2.7 times that injected into a human eye.

Administration of 1.25 mg (0.05 ml) and 2.50 mg (0.1 ml) of intravitreal bevacizumab showed no evidence of inner or outer retinal or optic nerve toxicity by light microscopy at one month in this rabbit model. Early reports of the use of intravitreal bevacizumab in VEGF-mediated diseases are encouraging.1–6 The effects of repeated injections and the half-life of bevacizumab in the vitreous are unknown and are presently under investigation.
REFERENCES


Evaluating Central Corneal Thickness Measurements With Noncontact Optical Low-Coherence Reflectometry and Contact Ultrasound Pachymetry

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PURPOSE: To compare the central corneal thickness (CCT) measurements obtained with noncontact optical low-coherence reflectometry (OLCR) and ultrasound (US) pachymetry.

DESIGN: Prospective, comparative observational study.

METHODS: Three sequential ultrasonic measurements and a set of five OLCR scans of 52 eyes of 26 healthy subjects were recorded. Noncontact measurement was repeated five minutes after anesthetic drop installation.

RESULTS: Mean CCT values for noncontact OLCR and US pachymetry were 544.03 μm and 548.66 μm, respectively, with mean SDs of 0.97 μm and 4.63 μm, respectively. Noncontact OLCR measured on average 4.64 μm less than US pachymetry (95% confidence interval −7.56 to −1.72; P = .003). The OLCR measured 1.68 μm less than US pachymetry in the thinner cornea group (<548.7 μm, n = 24) and 7.48 μm less in the thicker group (n = 25). This difference was statistically significant (P = .04).

CONCLUSIONS: There was agreement between the two pachymetric measurements. Noncontact OLCR appeared to measure slightly smaller than US pachymetry. (Am J Ophthalmol 2006;142:164–165. © 2006 by Elsevier Inc. All rights reserved.)

CENTRAL CORNEAL THICKNESS (CCT) DETERMINATION has become essential in corneal refractive surgery and glaucoma patient management.1 Ultrasound (US) pachymetry has been the current standard for CCT measurement. The purpose of this study is to compare the CCT of normal human corneas measured with noncontact optical low-coherence reflectometry (OLCR) vs contact US pachymetry. We also evaluated the CCT five minutes after anesthetic drop instillation to assess its effect on the OLCR pachymetric analysis.

CCT of 52 eyes of 26 patients was measured at our center. This study was approved by the institutional review board, and each patient provided informed consent. The mean age of patients was 38 years ± 9.9 (mean ± SD) with a male/female ratio of 14:12. Mean manifest refraction spherical equivalent was −4.07 diopters ± 2.56 (range −10.50 to +0.25 diopters). All patients had unremarkable ocular history and had not worn contact lenses for at least 24 hours. In the following sequence, OLCR (Pachimeter, Haag-Streit AG, Koeniz, Switzerland) (Figure 1) immediately followed by US pachymetry (DGII500 Pachette; DGH Technology Inc, Exton, Pennsylvania, USA) and a second set of OLCR measurements five minutes after US pachymetry was performed on each study eye. Final CCT measurements comparing the two pachymetry methods were available in 49 eyes of 26 patients. Thirty-nine eyes of 20 patients were studied to compare the thickness before and five minutes after anesthetic drop instillation by OLCR pachymetry. All of the measurements were taken between 10:00 am and 4:00 pm.

The principal operations of the OLCR and US pachymetry used in this study have been described elsewhere.2,3 Briefly,