Collagen shields and intraocular drug delivery: concentration of gentamicin in the aqueous and vitreous of a rabbit eye after lensectomy and vitrectomy

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Accepted 3 October 1991

Key words: collagen shield, vitrectomized and lensectomized rabbit eyes, gentamicin, drug delivery

Abstract

Five albino New Zealand rabbits underwent bilateral lensectomy and vitrectomy. All left eyes were fitted with a collagen shield that had been soaked for 5 min in 2.0 mL of gentamicin solution (40 mg/mL for IV use). Right eyes were treated with fortified gentamicin drops (13.6 mg/mL) every 30 min for 12 hrs. Aqueous and vitreous specimens were obtained at the following time intervals: 1, 2, 4, 8, 12 and 24 hrs.

We found the gentamicin concentrations to be higher in the aqueous of all eyes treated with fortified gentamicin drops. Only those eyes treated with fortified gentamicin drops attained a therapeutic drug level (4 μg–9 μg/mL) in the aqueous. Therapeutic drug levels were not attained in the vitreous of either treatment group.

Introduction

The administration of ocular antibiotics has been carried out in the past in many ways. The use of frequent topical drops [2], fortified topical preparations [3, 11], fortified ointments [9], subconjunctival injections [2], and intraocular injections [16] has been described, dependent on the type of infective process. More recently hydrophilic contact lenses soaked in water-soluble gentamicin solutions [5] have been shown to be very effective in providing a therapeutic drug level in the tear film for an extended period of time with much less patient morbidity and discomfort. Hydrophilic contact lenses have also been used to attain higher intraocular drug levels [13, 22].

Collagen shields have been shown by many studies to promote epithelial healing after surgical procedures involving the anterior segment [12, 19]. It has also been demonstrated that collagen shields may be hydrated in highly concentrated solutions of tobramycin [21], as well as such drugs as gentamicin, dexamethasone, pilocarpine and flurbiprofen, and then placed on the surface of the cornea with no significant signs of toxicity or adverse effect to the eye [1]. More importantly, it appears that these antibiotic (tobramycin/gentamicin) soaked collagen shields deliver a higher concentration of antibiotic to the cornea and aqueous humor in the rabbit eye in comparison to subconjunctival injections [21] and fortified drops [18]. This increased level of antibiotic concentration is seen not only at the outset, but appears to persist for at least 4 hrs before tapering to a similar level at approximately 8 hrs [21]. It is also important to note that although the actual amount of tobramycin contained in the collagen shield is much less than that injected subconjunctivally, higher concentrations are achieved in the cornea and aqueous [21]. In a further study, Hobden and associates using rabbit eyes infected with Pseudomonas aeruginosa demonstrated that once the collagen shield had been soaked in tobra-
mycin solution and placed on the eye, administering 4 drops of 4% tobramycin solution over the shield 5 hrs after its initial placement caused a significant reduction of bacterial colony-forming units in the cornea, similar to the effect of replacing the collagen shield with one newly hydrated [8]. Therefore, the collagen shield appears to act as a reservoir, prolonging the contact of the antibiotic with the ocular surface, allowing increased absorption and resulting in sustained concentration levels.

All of these studies were primarily concerned with the absorption of antibiotic in the cornea and anterior chamber. We were interested in determining if the increased and sustained concentration levels can also be observed in the vitreous. Intravitreal injection has previously been proven to be the most effective method of intraocular drug delivery [17]. A significant amount of patient discomfort is caused by this procedure. Intravitreal injection requires patient cooperation and often an operating room. Antibiotic-hydrated collagen shields would be much easier to use for the treatment of endophthalmitis. Our study was undertaken to compare the concentration of gentamicin in the aqueous and vitreous achieved with the use of a gentamicin-soaked collagen shield with the concentration achieved by the use of fortified topical drops in a lensectomized and vitrectomized rabbit eye.

Materials and methods

Five albino New Zealand rabbits weighing approximately 2–3 kg each were anesthetized using an intramuscular injection of 30 mg/kg body weight of ketamine HCl and 3 mg/kg body weight of xylazine for all procedures. Topical proparacaine HCl 0.5% was instilled into each study eye prior to any surgical procedure.

After anesthesia and akinesia were established, each rabbit was placed in the supine position and a wire lid speculum was inserted to keep the eye open. The eyes were dilated using 1 drop of each of the following: phenylephrine HCl 2.5%, tropicamide 1.0% and cyclopentolate 1.5% topical drops. All surgical procedures were carried out using the usual aseptic surgical protocol. A small superior limbal peritomy was created, extending from approximately the 10 o’clock to the 2 o’clock position. The conjunctiva was then dissected back and bleeding vessels were cauterized using a disposable hand-held cautery. The MVR blade was used to create a stab incision through the pars plana, approximately 1.5 mm behind the limbus in the superotemporal quadrant. Another stab incision was created in the superonasal quadrant 1.5 mm behind the limbus. A 25-gauge butterfly needle was inserted through this incision and was hooked up to the infusion solution consisting of commercially prepared balanced salt solution (BSS Plus) with the following additives: gentamicin 4.0 mg/mL, dexamethasone 64 µg/mL and intracardiac epinephrine (1:1,000) 1.0 mL/500 mL bottle. The infusion rate was controlled in order to maintain intraocular pressure throughout the procedure. Using the fragmotome and Peyman vitrophage, the entire lens was removed via the pars plana approach. Particular attention was given to the removal of the anterior capsule. Once the entire lens was removed, a core vitrectomy was carried out. The peripheral vitreous was not excised. At the end of the procedure, 1.0 mg of intraocular dexamethasone was administered. The stab incisions were closed using 8-0 vicryl suture, ensuring that the wounds were watertight. The conjunctiva was brought forward and placed at the limbus. Subconjunctival gentamicin 4.0 mg/0.1 mL was administered. Atropine ointment 1.0% was instilled into the fornix of the operated eye and the eye was patched shut.

This same procedure was initially carried out on one eye of each of the five rabbits. These rabbits were examined the following day, ensuring that there was good red reflex with no clinical signs of endophthalmitis. The patch was removed. The rabbits were examined weekly. Two of the initial rabbits developed endophthalmitis in the ensuing period and had to be sacrificed. They were replaced with two similar rabbits. Once there appeared to be good healing in all the operated eyes (approximately two weeks later), this same procedure was repeated in the other eye of all rabbits.

The second phase of the experiment began three months after the initial procedure. All study eyes