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EFFECT OF INTRAOCULAR POVIDONE-IODINE SOLUTION IN PREVENTION OF BACTERIAL ENDOPHTHALMITIS IN A RABBIT MODEL

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ABSTRACT

In order to determine the effects of intraocular 0.05% povidone-iodine preparation in the prevention of bacterial endophthalmitis in a rabbit model, 28 albino rabbits were randomly assigned to 4 equal groups. A concentration of 5×10^8 organisms (0.03 mL) in logarithmic growth phase of *S. epidermidis*, *S. aureus*, *Proteus mirabilis* and *Pseudomonas aeruginosa*, were injected separately in the anterior chamber of right and left eyes of each group. Then 0.03 mL of 0.05% povidone-iodine solution was injected in the left eyes. Eye examinations were performed with a slit-lamp daily for two weeks following injection.

From 28 eyes injected with bacteria and povidone-iodine, 20 cases did not develop endophthalmitis, one developed mild, one developed moderate, and 6 developed severe endophthalmitis. In comparison, from 28 eyes injected with bacteria and balanced salt solution, 9 cases developed mild, 10 developed moderate and 9 developed severe endophthalmitis ($p<0.001$) .

Povidone-iodine solution is therefore effective in prevention of bacterial endophthalmitis, although its efficacy has a direct relationship to the bacteria type and species.

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INTRODUCTION

Bacterial endophthalmitis is a disastrous and serious complication of intraocular surgery, and even with new and aggressive methods of therapy the patient does not gain useful vision in many cases.[1,2] At the end of the 19th century the rate of infectious endophthalmitis after intraocular surgery was about 10 percent, from 1900 to 1925 the rate was about 1.8%, from 1925 to 1950 about 0.58% and after 1950 on the average about 0.35% (range 0.05%-0.7%).[3,4] The complexity of intraocular procedures is increasing from day to day.[5] Utilization of intraocular lenses, corneal preservation, vitreous surgery techniques, surgical instruments and various fluids which are used for intraocular infusion, increases the potential sources of post-surgical endophthalmitis.[6] Nowadays, preparation of eyelids and conjunctival tissues with povidone-iodine, prophylactic use of local antibiotics and subconjunctival injection of broad-spectrum antibiotics at the end of surgery are used for prevention of postsurgical endophthalmitis.[7,8] Only through evaluation of the ocular changes associated with specific bacteria and the host's response to the offending organism will we better understand the interplay between the bacterial organism, the secondary ocular inflammatory responses, and the potential toxicity of intraocular medications.[9,10]

This study is based on the development of bacterial endophthalmitis in a rabbit model and examination of the effects of 0.05% intraocular povidone-iodine in the prevention of bacterial endophthalmitis.

MATERIALS AND METHODS

56 eyes of 28 white rabbits weighing 2.0 to 2.5 kg were used in this study. A concentration of 5×10^8 organisms (0.03 mL) in logarithmic growth phase of *S. epidermidis*, *S. aureus*, *Proteus mirabilis* and *Pseudomonas aeruginosa* organisms was prepared by Razi Institute of Tehran.

0.05% Povidone-iodine solution was prepared, and corneal endothelial cell count was done with specular microscopy.

28 white rabbits were randomly divided into 4 equal groups: A,B,C and D. Each rabbit was anesthetized with intramuscular ketamine (25 mg/kg) and atropine (0.5 mg).

0.03 mL of each bacterial species suspension (Group A: *S. epidermidis*, Group B: *S. aureus*, Group C: *Proteus mirabilis*, Group D: *Pseudomonas aeruginosa)* was injected into the anterior chamber of right and left eyes, then 0.03 mL povidone-iodine (0.05%) was injected into the right eye's anterior chamber and 0.03 mL BSS (balanced salt solution) was injected into the left eye's anterior chamber. All intraocular injections were done with a 27-gauge needle from the supratemporal part of the limbus. After each injection, the needle was removed and a cotton-tipped applicator was placed over the injection site for 1 minute.

After injection, each rabbit was examined with a slit-lamp and the red reflex was checked daily for 2 weeks.

After 2 weeks, corneal endothelial cell count was performed with a Pro/Koester Alcon wide field scanning corneal microscope. In some cases endothelial cell count was impossible due to corneal edema or perforation.

Daily eye examination was done with respect to the following factors:[13,14]

1. Presence or absence of conjunctival injection and/or chemosis (Grading 0-4).
2. Presence or absence of corneal clarity (Grading 0-4)
3. Anterior chamber reaction (Grading 0-4).
4. Degree of vitreous opacification (Grading 0-4).
5. Red reflex (Grading: full, decreased, yellow, absent).

Classification of endophthalmitis was done on the basis of the degree of vitritis (vitreous opacity) and red reflex (full, decreased, yellowish, absent).[11,14]

RESULTS

Before randomization and grouping of rabbits and intraocular injections, corneal endothelial cell count was done. There was no significant difference in the corneal endothelial cell count of rabbits before injections. The number of endothelial cells was 2700 -2800 (mean: 2750) per mm^2. After the injections the following results were observed:

Group A: None of the right eyes (*S. epidermidis* +Betadine injection) developed endophthalmitis. All left eyes (*S. epidermidis* + placebo injection) developed mild endophthalmitis. Two weeks after intraocular injection, the mean corneal endothelial cell count of right eyes was 2464 ± 51 (10.4% decrease in endothelial cells) and of left eyes was 2089 ± 69 (24.2% decrease). This difference has statistical importance (2-tailed $p < 0.01$, df=12, t=12.1).

Group B: None of the right eyes (*S. aureus* + Betadine injection) developed endophthalmitis. But from among the left eyes (*S. aureus* + placebo injections), two cases developed mild endophthalmitis (B1,B3,B4,B6,B7). Two weeks after injection the mean corneal endothelial cell count of right eyes was 2343 ± 49 (14.8% decrease in endothelial cells). From among the left eyes 2 cases (B2, B5) showed a 31% decrease in endothelial cell count. Because of corneal edema in the other cases, endothelial cell counting could not be done.

Group C: One case of right eyes (*Proteus mirabilis* + Betadine injection) developed mild endophthalmitis while the others fared well. Five cases of left eyes (C2,C4,C5, C6, C7) developed moderate and two (C1, C3) developed severe endophthalmitis. Two weeks after injection the mean corneal endothelial cell count of right eyes was 2250 ± 189 (18% decrease in endothelial cells). Because of severe corneal edema in the left eyes, endothelial cell counting could not be done.

Group D: One case of right eyes (*Pseudomonas aeruginosa* + Betadine) developed moderate and the others developed severe endophthalmitis. All left eyes developed severe endophthalmitis. Due to severe corneal edema or corneal perforation, corneal endothelial cell counting could not be done.

Overall, from 28 right eyes (bacterial species + Betadine injection) one case developed mild endophthalmitis, one moderate, 6 severe and 20 did not develop endophthalmitis. From 28 left eyes (bacterial species + placebo injection), nine developed mild, ten moderate and nine developed severe endophthalmitis. The differences between right (bacterial species + Betadine) and left eyes (bactereal species + placebo) are statistically significant ($p<0.001$, df =3, $\chi^2=34$.

DISCUSSION

Bacterial endophthalmitis is a serious and disastrous complication of intraocular surgery, and even with modern and aggressive methods of therapy, the patient may not gain useful vision in many cases.[1,2] Most cases of infectious endophthalmitis occur after intraocular surgery.[1] Since cataract surgery with placement of intraocular lenses is the most common intraocular procedure performed today, endophthalmitis most frequently occurs after this type of surgery. Although many efforts have been made to decrease the rate of postoperative infectious endophthalmitis, its rate

is still approximately 1/1000.[3,7,12] The clinical presentation of endophthalmitis is determined by the clinical category, the relative severity, the infecting organism and the elapsed time since the initiation of infection.[7] Povidone-iodine used as a topical antimicrobial agent has been reported to be effective in treating conjunctivitis and keratoconjunctivitis,[21,22] and has been used effectively in decontamination of donor corneas.[23] It has been suggested that the small amount that might be washed from the conjunctival sac into the eye during an intraocular procedure does not damage the corneal endothelium;[24] however, larger doses are toxic to the endothelium (Scott MacRae, MD, personal communication). Povidone-iodine placed in the conjunctival sac before intraocular surgery caused no significant effect on endothelial thickness or cell count compared with controls.[24] In a study done by Gocke, 230 clinical isolates were surveyed for susceptibility to povidone-iodine (Betadine). All isolates were completely killed after 120 seconds of contact with Betadine. A paradoxical increase in killing activity by lower concentrations of Betadine was observed (maximal killing at about 0.1% solution). A new formulation (SP-Betadine) was completely fatal for all isolates after only 15 seconds of contact time.[20] 0.1% Betadine solution has no cell toxicity while full bactericidal activity persists.[15] Betadine is an effective broad spectrum disinfectant with no reported toxicity to the cornea and conjunctiva when applied topically in the treatment of conjunctivitis and keratoconjunctivitis.[16-18] A study done in 1990 on rabbit eyes by Whitacre and Crockett showed that intravitreal injection of 0.1 mL of 0.05% povidone-iodine solution had no toxicity on the cornea, retina, or lens and no detectable pathologic or ERG changes were found.[19] Povidone-iodine has broad-spectrum bactericidal activity[25,26] and, unlike antibacterial antibiotics is also effective against fungi[27,28] and several viruses,[29] including the human immunodeficiency virus.[30] It works rapidly to kill most bacteria within 15 to 30 seconds and has sustained activity by slowly releasing free iodine from the povidone organic complex.[26-28] With respect to the high bactericidal activity and low side effects of povidone-iodine, this study was done to evaluate the efficacy of povidone-iodine 0.05% solution in prevention of bacterial endophthalmitis. The results show that intraocular injection of povidone-iodine in a concentration that has no significant side effects for the eye (0.03 mL of 0.05% Betadine solution) can prevent bacterial endophthalmitis. This study also shows that the efficacy of povidone-iodine in prevention of endophthalmitis has a direct relation to the type and species of infecting bacteria.

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