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Study of the Acute Effects of Povidone–Iodine on Conjunctival Bacterial Flora

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Abstract

Purpose: The purpose of this laboratory study was to assess the effect of povidone–iodine (PI) use topically on the conjunctiva in regard to needle bore contamination and to compare these results with our previous findings from an evaluation of bacterial contamination following gatifloxacin and moxifloxacin administration.
Methods: We performed 100 conjunctival 27-gauge needle penetrations of both eyes of 13 fresh cadavers. Eyes were then soaked in 10% PI, after which conjunctiva was again penetrated 100 times. After conjunctival penetration, the needles were irrigated, and the irrigant was assessed for bacterial growth. Results were compared with previous work assessing fluoroquinolone effectiveness through the same model.
Results: We observed a 28% ($P = 0.003$) decrease in bacterial growth and 40% ($P < 0.0001$) decrease in colony counts after PI placement. Differences between the effect of PI versus moxifloxacin and gatifloxacin were not statistically significant.
Conclusions: There is a greater decrease in bacterial load after treatment with PI for surface cultures than for cultures obtained through a needle bore passed through the conjunctiva. PI is a superior approach to topical antibiotics to decrease conjunctival bacterial load.

Introduction

As do all mucous membranes in the body, the conjunctiva carries a large bacterial load on its surface. The human bacterial biome is increasingly understood as an important part of our survival mechanism, especially when we have a healthy bacterial layer. However, there are times when it is important to decrease this bacterial load to decrease the risk of infection. This is certainly true for intraocular surgery, where resultant infections closely mirror bacteria found on the conjunctival surface and in the tear film.[1–3] With the large clinical burden of administering intraocular injections, a decrease of conjunctival bacterial burden also is important because the risk for infection is most likely closely related.

Exactly how bacteria are introduced into the eye after intraocular injection is not clear, although it could be either due to exposure of the needle site to conjunctival, lid, or meibomian gland flora or a result of respiratory flora that are on the needle during injection.[4–20] Alternatively, this could be due to bacteria, which are found in the needle bore as it penetrates the conjunctiva and then are introduced into the eye with the injection. Another possibility is bacterial contamination of the injection site or of prolapsed vitreous from the site, although with the techniques used today, either of these causes would seem very unlikely. Previously, we have shown that bacterial contamination in the bore of the needle is common after penetrating the conjunctiva in fresh cadaver specimens and that preinjection use of topical 0.3% gatifloxacin and 0.5% moxifloxacin has a small but significant decrease in this contamination rate.[21]

This study looks at the impact of 10% topical povidone–iodine (PI) on needle bore contamination and then compares this effect with our previous findings.[21]

Methods

We conducted this study with 13 consecutive fresh cadavers consented for tissue harvesting, using the same protocol as the one we followed in our previous study.[21] We used ten 27-gauge needles to penetrate the conjunctiva 10 times each, for a total of 100 conjunctival penetrations in each eye. Following this procedure, we stored the needles in a sterile container. Then, both eyes were soaked in 10% PI for 10 min. After irrigating away the PI, we used 10 additional 27-gauge needles per eye to penetrate the conjunctiva 10 times each for 100 conjunctival penetrations per eye, with the needles again stored separately in a sterile container.

Each needle was irrigated with 1.0 mL of sterile saline, with the irrigant evenly spread on a blood agar plate and

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incubated at 37°C. After the plates were incubated for 7 days, they were inspected and scored as having either no growth or growth, and the total number of colonies was determined.

We used a chi-square analysis to compare the differences in positive cultures between pre- and postplacement of PI, with significance set at $P < 0.01$ after a Bonferroni correction for multiple comparisons.

Results

One hundred eighteen of the 260 agar plates were positive for growth before PI placement, while 85 of 260 agar plates were positive for growth after PI placement, for a net decrease of 28.0% ($P = 0.003$). The total number of colonies before and after PI was 1,467 and 879, respectively, for a net reduction of 40.1% ($P < 0.0001$).

When we compared the decrease in growth after PI with our previous study findings,[21] the net decrease was 28.0% for PI, 24.2% for moxifloxacin, and 11.7% for gatifloxacin. These differences were not statistically significant.

Discussion

While it is accepted that endophthalmitis is a serious complication of intraocular injections, which can lead to loss of useful vision, the incidence of this problem is <0.1%.[5–20,22] However, many patients with multiple injections may run a sequential risk of several percent; thus, the lifetime risk is not inconsequential and prophylaxis is an important area of interest. Currently, there is wide disagreement about what represents best practice. Our study suggests that topical PI may decrease the risk of vitreal contamination by ~28%–40% with a 10% solution. Given that lower concentrations of PI are routinely used clinically, we expect this to be the maximum decrease in a clinical setting. Depending on the bacterial pathogenicity and whether the total colony formation or injection of any bacteria best correlates with the actual onset of endophthalmitis, these factors could be important.

Friedman et al. recently looked at conjunctival cultures in patients and determined that treatment with 5% PI for at least 30 s resulted in about a 50% decrease in the incidence of positive cultures in patients. This decrease in positive cultures, along with a 75% to >90% decrease in colony-forming units, occurred after only 60 s of soaking.[23] This effect was observed with 5% rather than 10% PI, is substantially greater than the effect that we documented, and took place after only 1 min of soaking with 5% rather than 10% PI. First of all, it should be noted that our study did not replicate the clinical setting as 10 min of treatment with 10% PI is typically not used for patient care due to the risk of ocular irritation. Furthermore, even with intraocular surgery, 10 min of soaking the conjunctival surface with PI also is unlikely to occur and tears would dilute this concentration in patients, even with intraocular surgery. Although we would expect our study to indicate the maximal effect one could expect from PI, the results of the Friedman study showed a dramatically greater effect when the conjunctival surface was cultured with a cotton-tipped applicator.

One explanation of our study results as well as of many other findings, which show a dramatic effect with topical PI,[24–36] is that culturing the conjunctival surface may not correlate with the total conjunctival bacterial load due to the many bacteria-laden folds and crypts in the conjunctiva. Furthermore, since residual antiseptic or antibiotic is most likely to be in the tear film, the superficial bacterial load is most likely to be less than that found in the folds and crypts of the conjunctiva. For instance, it was once standard procedure to vigorously irrigate the conjunctival surface with copious amounts of saline solution to try and decrease the total bacterial burden. Once cultures were taken to validate this practice, it became clear that the irrigation actually increased the bacterial load in the tear film due to the hidden bacteria now displaced from the conjunctival folds.

By passing a hypodermic needle through the conjunctiva, our sampling procedure would resemble a bacterial biopsy of the conjunctiva and thereby would avoid the problem of a more sterile tear film than would be found deeper in the conjunctiva structure. A study to show that this correlates with endophthalmitis has not been performed and would be daunting due to a variety of technical and logistical factors. However, any bacteria trapped in the needle bore and irrigated onto an agar plate would also be irrigated into the vitreous humor, where tissue has a minimal ability to fight infection. While our testing was with a 27-gauge needle and much smaller needles are generally used today, in our previous study, we did include a cohort tested with a smaller needle and this did not result in a significant decrease in the number of needles that were contaminated after passing through the conjunctiva.

Many have questioned the efficacy of topical antibiotics for prophylaxis with intraocular injections.[37,38] While we did not see a significant difference between the use of topical PI and 0.3% gatifloxacin or 0.5% moxifloxacin, soaking the surface of the conjunctiva, our study, without any tear flow or tear reflex for 10 min is also not clinically comparable. Furthermore, studies have shown that topical antibiotics result in an increase in resistant organisms[39–41]; so, for all the reasons we have listed, PI would seem to be a superior approach. Combining topical PI with topical antibiotics before intraocular injection is one approach that may prove synergistic, but this has not been studied in detail.

Weaknesses of this study include the sampling of cadavers; however, most were eyes that were designated for research and that had to be harvested within 4 h of death. The relative effect of PI on conjunctival bacterial load is likely to be similar, even though the actual bacterial load in cadaver eyes probably differs from that which is present in our patients. Knowing that there is a symbiotic homeostasis with the bacterial biome on human mucous membranes suggests that great change in the bacterial load over a few hours is unlikely. In any event, our main interest is the relative impact of topical PI when the total thickness of conjunctiva is sampled, which is what would occur with a needle penetration, and this should not be impacted substantially in fresh cadavers when compared with living patients.

We also recognize that clinical settings utilize 30-gauge needles rather than the larger bore 27-gauge needles used in the study. We expected that by utilizing the same puncture technique, a larger bore would result in a higher bacterial contamination rate; however, the rate was the same with both needle sizes when compared with our previous 30-gauge study. Although 27 gauge is not typically used clinically, this refutes the assumption that larger bore needles may be less safe with respect to bacterial inoculation.

In conclusion, we were able to show that when the conjunctiva in fresh cadavers is sampled through its full thickness with a needle, topical 10% PI for 10 min resulted in a 28% decrease in positive cultures and a 40% reduction in total colonies cultured. This effect is substantially less than what is observed when surface cultures are taken in patients. We feel our study calls into question whether surface cultures adequately sample the full conjunctival bacterial load and which bacterial load is more relevant to a hypodermic needle passing through the conjunctiva. We agree that topical PI is the best approach in decreasing the bacterial burden of the conjunctiva, but expect a maximal effect is not likely to be more than a 40% decrease risk of endophthalmitis. While prospective randomized trials would be the only way to resolve this question, such studies are unlikely to be forthcoming as they would be very large due to the low incidence of endophthalmitis after intraocular injections.

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Author Disclosure Statement

No competing financial interests exist.

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