

## Prophylaxis Against Endophthalmitis in Cataract Surgery

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### Abstract

**Introduction:** Endophthalmitis is an uncommon but potentially devastating complication of cataract surgery and often carries a poor prognosis. The incidence of endophthalmitis varies considerably in the literature, ranging from 0.05% to 0.35%. Some measures routinely used as prophylaxis have not been proven to be of benefit. This article reviews the current literature on the common prophylactic measures used to prevent endophthalmitis. **Methods:** A search of the literature in Medline and critical review of the study design, sample size, and analysis of outcomes. **Results:** Clinical studies on prophylactic measures suggest that using povidone-iodine 5% to clean the eyelids and conjunctiva before cataract surgery has a significant benefit both in reducing the actual rate of endophthalmitis and reducing the bacterial load after surgery. A bolus dose of intracameral cefazolin or cefuroxime has a significant benefit on reducing infection rate, with evidence for the latter drug coming from a large, prospective, randomised clinical trial. There is some evidence to suggest that subconjunctival antibiotics may reduce the incidence of endophthalmitis, although much of the evidence comes from case-control studies. Although the current evidence on the efficacy of topical antibiotic drops is mixed, this is commonly practiced both pre- and postoperatively. **Conclusions:** The most useful prophylactic measures to reduce the rate of endophthalmitis are the use of 5% povidone-iodine and intracameral injection of antibiotics after surgery. Subconjunctival antibiotics may be of benefit, while topical antibiotics alone may not reduce the rate of endophthalmitis significantly.

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### Introduction

Endophthalmitis is an uncommon but potentially devastating complication of cataract surgery and often carries a poor prognosis. Due to variations in study design and methods of data collection, as well as real differences in incidence among various centres, the reported rates of endophthalmitis vary considerably, ranging from 0.05% to 0.35%.<sup>1-6</sup> Ophthalmic surgeons have adopted various measures to reduce the incidence of postoperative endophthalmitis, although the evidence of the efficacy of some of these measures is not well established. This article reviews the current literature on the common prophylactic measures used to prevent endophthalmitis.

### Common Prophylactic Measures Against Endophthalmitis

The various measures adopted to reduce the rate of endophthalmitis vary considerably among different healthcare systems, institutions, and even individual sur-

geons.<sup>7-9</sup> Preoperatively, the measures currently used by surgeons include instillation of topical antibiotic eyedrops<sup>7-9</sup> and cleaning the lids and conjunctiva with chlorhexidine or povidone iodine.<sup>7,8</sup> Intraoperatively, antibiotics may be added to the irrigation fluid or given as a bolus intracameral dose at the end of surgery.<sup>7,8</sup> The common postoperative measures include subconjunctival injection of antibiotics<sup>7-9</sup> and topical antibiotic drops.<sup>7-9</sup>

### Preoperative Antiseptic Preparation

A case-control study in Western Australia found that preoperative antiseptic preparation reduced the risk of endophthalmitis [odds ratio (OR), 0.19].<sup>10</sup> Montan et al<sup>6</sup> reported a significant reduction in bacterial flora after rinsing the conjunctiva with 10 mL chlorhexidine 0.05%. Another study by Barkana et al<sup>11</sup> comparing the efficacy of preoperative povidone-iodine 4%, ofloxacin 0.3% and chlorhexidine 0.05% found no difference in the reduction of conjunctival bacterial flora among the 3 solutions.

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However, a prospective study in Thailand found that 82.4% of patients had positive cultures after cleaning the face with 4% chlorhexidine alone.<sup>12</sup>

### Povidone-Iodine

Povidone-iodine, which is bactericidal, is a complex polymer of polyvinyl pyrrolidine and iodine. It is believed to play an important role in reducing the rate of endophthalmitis and there is strong evidence to support its use.<sup>1</sup> In surveys of prophylactic measures taken by cataract surgeons to prevent endophthalmitis, a high proportion of respondents (between 69.8% and 99.5%) used povidone iodine preoperatively.<sup>7,8</sup>

In a systematic review of the literature from 1966 to 2000 on the efficacy of endophthalmitis prophylaxis techniques, preoperative povidone-iodine was the only measure to receive the intermediate clinical recommendation (moderately important to clinical outcome).<sup>13</sup> In that review, all other reported prophylactic interventions, including preoperative topical antibiotics, antibiotic-containing irrigating solutions, and postoperative subconjunctival antibiotic injection received the lowest clinical recommendation (possibly relevant but not definitely related to clinical outcome).<sup>13</sup>

There are several studies which document a lower rate of endophthalmitis when povidone-iodine is used to clean the surrounding skin, eyelids or conjunctiva. In a non-randomised study, topical 5% povidone-iodine was applied onto the ocular surface before transferring the patient into the operating theatre. The endophthalmitis rate in this group was lower (4 of 4089 eyes, 0.097%) compared to a group of patients not receiving povidone-iodine the previous year (9 of 3052 eyes, 0.294%) and during the period of the study (1 of 502 eyes, 0.199%).<sup>14</sup> A retrospective review of 19,269 consecutive cases of cataract surgery reported a lower rate of endophthalmitis (0.03%) during the period 1990 to 1996 when the use of povidone-iodine was implemented compared to 0.08% in the preceding period from 1986 to 1989.<sup>15</sup> In a cross-sectional survey of 469 centres in Germany which performed 340,663 cataract surgeries in total, Schimtz et al<sup>16</sup> reported that application of povidone-iodine on the conjunctiva preoperatively reduced the risk of endophthalmitis [OR, 0.59; 95% confidence interval (CI), 0.36-0.99]. Thoms et al<sup>17</sup> reviewed the incidence of endophthalmitis in 815 consecutive cataract surgeries over a 5-year period and reported a significantly higher incidence of endophthalmitis in patients who did not receive 5% povidone-iodine drops immediately after wound closure.

It has been suggested that a higher concentration of povidone-iodine applied to the skin may have a greater effect on prevention of endophthalmitis. A retrospective,

comparative, case-controlled study reviewing medical charts of 10,614 extracapsular cataract extraction surgeries performed between 1992 and 2000 reported that a lower risk of endophthalmitis was associated with conjunctival disinfection with 5% povidone-iodine and with skin preparation using 10% instead of 5% povidone-iodine.<sup>18</sup>

Several studies have demonstrated a decrease in the proportion of positive cultures from conjunctival swabs taken after application of povidone-iodine to the conjunctiva or skin compared to pre-treatment swabs.<sup>11,12,19-22</sup> Although some centres use povidone-iodine drops, Safar et al<sup>23</sup> reported that bacterial colonisation was lower when 5% povidone-iodine was used to irrigate the conjunctival fornix compared to instillation of drops. Ferguson et al<sup>24</sup> demonstrated that 5% povidone-iodine is more effective than 1% povidone-iodine in decreasing human conjunctival bacterial flora *in vivo*. In a prospective study, Isenberg et al<sup>25</sup> treated eyes after cataract surgery for 1 week with a broad-spectrum antibiotic (polymyxin B sulfate-neomycin sulfate-gramicidin) or povidone-iodine drops (1.25% to 2.5%) and compared the mean number of colony-forming units in both groups as well as an untreated control group. At 1 week, eyes treated with povidone-iodine had a significantly lower species count compared to the control group. There was no significant difference in the number of colony-forming units between the 2 treated groups at 1 week, but both treated groups had a lower mean number of colony-forming units compared to the untreated group.

Povidone-iodine is known to cause eye irritation and discomfort and may also cause corneal epithelial defects. In a study of 3052 eyes cleaned with 5% povidone-iodine, 6.6% reported moderate to severe but tolerable irritation after application.<sup>14</sup>

### Intracameral Antibiotics

Although practice surveys suggest that the use of intracameral antibiotics is relatively low (ranging from 3.6% to 16.2% of surgeons in the United Kingdom),<sup>7,8</sup> its use may become increasingly common, especially after publication of several recent studies. A questionnaire survey of 469 centres in Germany in 1996 analysed the rates of endophthalmitis and correlated them with practices in those centres. It was reported that the risk of endophthalmitis was reduced with the use of intraocular antibiotics (OR, 0.65; 95% CI, 0.43-0.98).<sup>16</sup>

Various drugs have been used as intracameral injections, including cefazolin,<sup>2,3</sup> cefuroxime<sup>4,6</sup> and vancomycin.<sup>1</sup> The choice of antibiotics is usually guided by the microbiological cultures and susceptibility results from previous studies and the investigators' local data.<sup>2,3,6</sup> Cefazolin, a first-generation cephalosporin, is chosen because of its broader spectrum of activity against gram-positive bacteria

compared to a second-generation cephalosporin such as cefuroxime<sup>2</sup> although to date there are no studies directly comparing the efficacies of both these drugs in reducing the rate of endophthalmitis.

In 2002, Montan et al<sup>6</sup> reported that the use of intracameral cefuroxime 1 mg lowered the rate of endophthalmitis significantly from 0.26% to 0.06%. The recently published European Society of Cataract and Refractive Surgery (ESCRS) multicentre study of postoperative endophthalmitis was a prospective, randomised, multicentre study of 16,603 patients undergoing cataract surgery. Using a 2 x 2 factorial design, patients were randomised to receive intracameral cefuroxime (1 mg in 0.1 mL of normal saline) and/or topical perioperative 0.5% levofloxacin drops. The study reported that the absence of intracameral cefuroxime was associated with a 4.92-fold increase in the risk of total postoperative endophthalmitis.<sup>4</sup> The rate of endophthalmitis for the group which did not receive either topical levofloxacin or intracameral cefuroxime was 0.345% compared to 0.049% for the group treated with both.

Romero et al<sup>2</sup> reported promising results after instilling intracameral cefazolin (1 mg in 0.1 mL of 0.9% saline) in the capsular bag after cataract surgery. The rate of endophthalmitis in this group of patients was reduced to 0.055% compared to 0.63% in the preceding 2 years, when intracameral antibiotics were not used. Garat et al<sup>3</sup> reported a statistically significant reduction in the rate of endophthalmitis from 0.37% to 0.031% after initiating the use of intracameral cefazolin at a concentration of 2.5 mg in 0.1 mL. This was calculated to give a final concentration of 8,000 micrograms per mL in the anterior chamber (assuming the volume of the anterior chamber is 0.3 mL), which exceeds the minimum inhibitory concentration (MIC) for microorganisms susceptible to cefazolin.

Although vancomycin is another drug that can be used, and has the added advantage of efficacy against enterococci, which cefuroxime does not cover, it is felt that this is a drug of "last-resort" and should be reserved for treatment of actual endophthalmitis and not in prophylaxis in order to reduce the rate of antibiotic resistance.<sup>1,3,6</sup>

### Antibiotics in the Irrigation Fluid

Instead of a bolus dose of antibiotic at the end of surgery, some surgeons add antibiotics, such as vancomycin or gentamicin, to the irrigating fluid.<sup>1,26,27</sup> Several studies have shown that the use of antibiotics in the irrigation fluid reduces the rate of positive cultures from anterior chamber aspirates. Beigi et al<sup>26</sup> reported that adding vancomycin (20 micrograms/mL) and gentamicin (8 micrograms/mL) significantly reduced the rate of positive anterior chamber aspirate cultures to 2.7% compared to 20% in the control group. In a study by Sobaci et al,<sup>27</sup> contaminated aqueous

samples were lower in eyes where vancomycin and gentamicin were added to the irrigation fluid compared to eyes with balanced salt solution alone (6.8% vs 21.1%; OR, 3.65). Mendivil et al<sup>28</sup> reported a lower rate of culture-positive aspirates in the groups that received vancomycin in the irrigation fluid compared to the control group.

Some studies have reported that the reduction in culture positive rates were not statistically significant. Ferro et al<sup>29</sup> performed a randomised study where 1 group of patients was operated using vancomycin (20 micrograms/mL) and gentamicin (8 micrograms/mL) while a control group had no antibiotics in the irrigating fluid. Although anterior chamber aspirates with positive cultures was higher in the control group (12% vs 5%; OR, 2.51), this difference was not statistically significant. In a non-randomised study, Feys et al<sup>30</sup> compared the anterior chamber aspirate cultures between a group of patients where vancomycin was added to the irrigation fluid with cultures from a control group without antibiotics and reported that there was no difference in the rate of culture positive aspirates between both groups.

### Toxicity of Intracameral Antibiotics

Although there is concern about the possible effects of toxicity of antibiotics on intraocular structures, in 2 studies using cefazolin at doses of 1 or 2.5 mg, no adverse events in terms of postoperative inflammation or visual acuity was reported.<sup>2,3</sup> In a prospective, randomised controlled trial investigating the possible effect of vancomycin (20 micrograms/mL) and gentamicin (8 micrograms/mL) in the infusion fluid during cataract surgery, there was no significant difference in increased macular thickness or contrast sensitivity at 5 weeks compared to the group that did not receive antibiotics.<sup>31</sup>

A study by Espiritu et al<sup>32</sup> concluded that adding intracameral moxifloxacin 500 micrograms in 0.1 mL at the end of phacoemulsification was not toxic in terms of visual acuity, anterior chamber reaction, pachymetry and endothelial cell count.

### Subconjunctival Antibiotics

Many surgeons give a bolus subconjunctival injection of antibiotics at the end of cataract surgery. Clinical practice surveys suggest that between 44.1% and 67.6% of surgeons routinely give subconjunctival antibiotics after cataract surgery.<sup>8,9</sup>

Most of the evidence for efficacy of subconjunctival antibiotics is derived from retrospective case-control studies which identify risk factor for endophthalmitis. In a retrospective chart review of 13,886 consecutive cataract surgeries, Colleaux and Hamilton<sup>33</sup> reported a significantly lower incidence of postoperative endophthalmitis when

subconjunctival antibiotic injections were given (0.011% vs 0.179%) (OR, 16.2; 95% CI, 1.9 to 137.1). A case-control study of 205 cases of endophthalmitis in Western Australia found that subconjunctival injection of antibiotics reduced the risk of endophthalmitis (OR 0.46; 95% CI, 0.29 to 0.70).<sup>10</sup> Lertsumitkul et al<sup>34</sup> reported similar findings in a study in Sydney. Lehmann et al<sup>35</sup> reviewed 9 cases of endophthalmitis over a 21-month period and compared them to 90 control patients. They found that none of the 9 endophthalmitis patients received preoperative subconjunctival cefuroxime compared with 43 of 90 control patients (47.8%). Krummenauer et al<sup>36</sup> performed a questionnaire survey of 538 centres in Germany and reported a significant benefit from intraoperative periocular antibiotics (OR, 0.68).

### Topical Antibiotics

A systematic review by Ciulla et al<sup>13</sup> gave the lowest clinical recommendation to preoperative topical antibiotics. Nevertheless, this is routinely prescribed by between 69.1% and 97.4% of surgeons in clinical practice surveys.<sup>8,9</sup>

The ESCRS Endophthalmitis Study Group reported an endophthalmitis rate of 0.251% in the group treated with levofloxacin 0.5% before and immediately after surgery compared to 0.326% in the group that received a placebo. However, regression analysis showed that the perioperative use of levofloxacin drops did not significantly reduce the risk of endophthalmitis.<sup>4</sup> Bohigian<sup>37</sup> compared the rate of endophthalmitis in 30,870 eyes treated with preoperative topical antibiotics and topical preoperative ciprofloxacin-soaked pledgets and reported no difference in the incidence of endophthalmitis.

A study by Lofoco et al<sup>38</sup> compared the rate of sterile cultures in 3 treatment groups: fusidic acid drops 1%, ofloxacin 0.3% and no treatment. Although there was no significant difference between the fusidic acid and ofloxacin groups, there was a significantly lower culture-positive rate in the treated compared to the untreated group. A similar study by Barkana et al<sup>11</sup> reported that ofloxacin 0.3% significantly reduced the number of colony forming units from cultures taken 3 minutes after treatment compared to the fellow eye.

With the introduction of fourth-generation fluoroquinolones (gatifloxacin and moxifloxacin), there has been interest in whether these drugs used topically might reduce the rate of endophthalmitis. These drugs prevent the action of both topoisomerase II and IV and achieve a high aqueous concentration after topical use.<sup>1</sup> A retrospective, multicentre, observational case series of 20,013 patients who had uncomplicated cataract surgeries by Moshirfar et al<sup>39</sup> reported an overall endophthalmitis rate of 0.07%. There was no significant difference in the rate of endophthalmitis

for gatifloxacin (0.06%) and moxifloxacin (0.1%).

A retrospective case-control study by Ng et al<sup>10</sup> reported that topical antibiotics before or after surgery did not significantly affect the rate of endophthalmitis. Another retrospective review of 13,886 consecutive cataract surgeries found that the incidence of endophthalmitis with and without preoperative use of antibiotic drops was not significantly different (0.066% vs. 0.115%).<sup>33</sup>

### Systemic Antibiotics

Systemic antibiotics are not commonly used as prophylaxis after cataract surgery. Schmitz et al<sup>16</sup> reported that the use of systemic antibiotics, when used solely in patients undergoing cataract surgery in an inpatient setting, reduced the risk of endophthalmitis, although the difference was not statistically significant.

### Conclusion

Clinical studies on prophylactic measures suggest that using povidone-iodine 5% to clean the eyelids and conjunctiva before cataract surgery has a significant benefit in reducing the rate of endophthalmitis and also reduces the rate of positive cultures from conjunctival swabs. A bolus dose of intracameral cefazolin or cefuroxime has a significant benefit on reducing infection rate, with evidence for the latter drug coming from a large, prospective, randomised clinical trial. There is some evidence to suggest that subconjunctival antibiotics may reduce the incidence of endophthalmitis, although much of the evidence comes from case-control studies. Although the current literature on the efficacy of topical antibiotic drops show mixed results, it is a common practice and likely to continue given the low risk of toxicity. It is important to note that all measures serve to reduce the rate of endophthalmitis, and no single measure can prevent its occurrence totally.

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*While every effort has been made to confirm the accuracy of dosages for medications and clinical outcomes reported in this review, readers are advised to confirm the appropriate drug dosage before treating patients. The author and the journal are not responsible for any errors in dosages or results reported.*

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