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Review

# Post-cataract surgery endophthalmitis: Brief literature review

Hesam Hashemian\*, Reza Mirshahi, Mehdi Khodaparast, Mahmoud Jabbarvand

*Ophthalmology Research Center, Department of Ophthalmology, Tehran University of Medical Sciences, Farabi Eye Hospital, Iran*

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## Abstract

**Purpose:** To investigate recent evidence in prophylaxis and management of post-cataract surgery endophthalmitis.**Methods:** We conducted a literature search using Pubmed database for post cataract surgery endophthalmitis, and relevant articles were selected from original English papers published since 2015.**Results:** Forty-nine articles were published regarding post-cataract surgery endophthalmitis from January 2015 to February 2016. A low incidence of post-cataract surgery endophthalmitis has been reported. A growing number of articles are focusing on preventing endophthalmitis using intracameral antibiotics.**Conclusion:** Based on the current evidence, intracameral antibiotics seems to be effective in preventing endophthalmitis after cataract surgery. Copyright © 2016, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).**Keywords:** Endophthalmitis; Microbiology; Risk factors; Post cataract surgery endophthalmitis

## Introduction

Endophthalmitis, although rare, is one of the most devastating complications of intraocular surgeries. As cataract surgery consists of a large fraction of ophthalmic operations, the majority of literature reports about the endophthalmitis is centered on cataract surgery.<sup>1</sup> An aging population worldwide necessitates an increase in the number of cataract surgeries, rendering post-cataract surgery endophthalmitis a public health concern.<sup>2</sup>

High morbidity and subsequent medical care expenses are part of this complication.<sup>2</sup> Visual outcomes are not often favorable; about 40% of affected patients sustain severe visual

loss (corrected distance visual acuity of less than 20/200), and only one-third of cases reach visual acuity of better than 20/40.<sup>3</sup> Evisceration as a last resort has also been employed in the case of endophthalmitis.<sup>4</sup>

The reported rate of post-operative endophthalmitis varies between a range of 0.04%–0.2%.<sup>5</sup> However, the incidence of post cataract surgery endophthalmitis shows significant changes overtime. By the time of introduction of clear cornea cataract extraction, as opposed to scleral or limbal incisions, an increase in endophthalmitis rate was observed.<sup>6–8</sup> There are also studies rejecting this hypothesis, with clear corneal technique being even a safer approach.<sup>9,10</sup>

## Methods

We reviewed recent literature using PubMed database to find original English articles with the keywords “endophthalmitis” and “cataract surgery” or “phacoemulsification”. The relevant articles for a comprehensive update were selected with a special focus on those published from January 2015 to February 2016.

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\* Corresponding author. Farabi Hospital, Qazvin Sq., Tehran, Iran. Tel.: +98 912 680 50 97; fax: +98 21 55409092.

E-mail addresses: [h-hashemian@tums.ac.ir](mailto:h-hashemian@tums.ac.ir), [shhlucky@yahoo.com](mailto:shhlucky@yahoo.com) (H. Hashemian).

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## Results

During the recent year, 49 articles were published on this subject. Sixteen articles were relevant for discussion in this review, of which 7 studies were retrospective and 3 of them were prospective. Also 4 case series, one prospective comparative interventional cohort study and one cost-effectiveness analysis were part of included studies. Intracameral antibiotic was the most prevalent subject discussed in these articles.

### Pathogen

Numerous fungal and bacterial agents can cause post-cataract surgery endophthalmitis, with gram positive, coagulase-negative *Staphylococci* being the most common. *Staphylococcus aureus* and *Streptococcus* species are often identified as causing factors as well.<sup>10–13</sup> This observation reflects the fact that aqueous contamination with surface bacterial flora is the main event in pathogenesis of endophthalmitis.<sup>14</sup> However, gram negative bacteria such as *Klebsiella pneumonia* may also be encountered occasionally, especially in Southeast Asia and in the older-age population based on Lundstrom et al's study.<sup>15</sup> *Candida albicans* is the most frequently isolated organism in the fungal category.<sup>16</sup> In recent years, *Enterococci* has emerged as the leading cause, most likely because of its relative resistance to cefuroxime.<sup>3,17</sup>

### Risk factors

#### Preoperative risk factors

Many conditions have been postulated as risk factors for the occurrence of endophthalmitis.<sup>18–32</sup> Advanced age (>85 years old), rural residence, male sex, and immunosuppressive states such as diabetes mellitus are proposed as patient-associated factors.<sup>2,7,8,15,18–20</sup> Performing cataract surgery on the same day rather than one day after admission may be accompanied by a higher risk of endophthalmitis.<sup>21</sup> In Nam et al's study, the spring season was an independent risk factor for the development of endophthalmitis.<sup>22</sup> A systematic review conducted by Cao et al identified age and male gender as the only preoperative risk factors.<sup>23</sup>

#### Intraoperative risk factors

Intracapsular and extracapsular cataract surgery, vitreous loss, and anterior vitrectomy are considered intraoperative risk factors. Silicone and polymethyl methacrylate (PMMA) intraocular lens (IOL) optic material compared to acrylic are associated with higher rates of endophthalmitis. However, the absence of an injector system for these IOLs and the need for a larger incision for non foldable PMMA lens can confound this association.<sup>10,19</sup> Based on Weston et al's study at 2015, injectable IOL is associated with a lower risk of endophthalmitis in comparison with forceps delivered IOL.<sup>24</sup> Concurrent eyelid or lacrimal surgery during the same hospitalization with cataract surgery can increase the risk of endophthalmitis significantly.<sup>25</sup>

#### Postoperative risk factors

Limited studies investigated post surgical events affecting the development of endophthalmitis. A number of risk factors have been proposed in control cohort and retrospective studies including starting topical antibiotics the day after surgery instead of the same day as surgery, not patching following surgery, and using older generations of fluoroquinolone antibiotics.<sup>26–28</sup>

Risk factors associated with postoperative endophthalmitis based on recent investigations is demonstrated in [Table 1](#).

#### Prophylaxis

The most important guideline on prophylaxis of endophthalmitis is based on the European Society of Cataract & Refractive Surgeons (ESCRS) study. This multicenter clinical trial was conducted on 16,603 patients in 4 arms using perioperative topical antibiotic, intracameral cefuroxime, and placebo.

According to this study, non-use of intracameral antibiotic, surgical complication, clear cornea incision as opposed to scleral tunnel, male gender, and implantation of silicon IOL were associated with a higher risk of endophthalmitis.<sup>19</sup>

In recent years, prophylaxis against endophthalmitis has evolved extensively. Suggested preoperative measures include lid hygiene for reduction of conjunctival flora and meticulous surgical prep and drape with topical povidone–iodine.<sup>33</sup> Nentwich et al investigated the role of copious irrigation of periorbital area and conjunctival sac with povidone-iodine in prevention of endophthalmitis, and based on a 19-year institutional experience, an 8-fold decrease in the rate of endophthalmitis was observed.<sup>34</sup>

The beneficial effects of preoperative lash trimming, saline irrigation, topical antibiotics, and antibiotic-containing irrigating solutions is not clearly established in reducing post operative rates of endophthalmitis.<sup>10,35–37</sup> However, Sharma et al found that intracameral concentration of moxifloxacin, whether used topically or orally, is sufficient enough for the prevention of proliferation of most bacteria causing endophthalmitis.<sup>38</sup> Subconjunctival antibiotics can be effective in minimizing the risk of endophthalmitis.<sup>10,21</sup> There is growing and compelling evidence supporting use of Intracameral antibiotic as one of the most effective countermeasures.<sup>2,10,11,39,40</sup> Studies show a 5- to 9-fold decrease in the rate of endophthalmitis via application of intracameral cefuroxime.<sup>19,41</sup> In addition, the relative low price of cefuroxime makes it cost-effective in preventing endophthalmitis.<sup>42</sup> Purslow et al also showed that commercially available intracameral cefuroxime, Apropam<sup>®</sup> costs less than the preparation of cefuroxime in hospitals.<sup>43</sup>

However, in 2015, Sharma et al reported the outcome of a randomized clinical trial regarding the effectiveness of intracameral cefuroxime, and they did not find any statistically significant additional benefit in preventing endophthalmitis.<sup>44</sup> These findings were clinically significant (the rate of endophthalmitis decreased from 0.155% to 0.108%) and in a larger sample size, they may be statistically significant as well.

Table 1  
Summary of recent studies evaluating rate, pathogen, and risk factors associated with post-cataract surgery acute endophthalmitis.

Authors, year [Ref]	Country	Date	Endophthalmitis rate	Pathogen	Risk factors
Jabbarvand et al, 2015 <sup>2</sup>	Iran	2006–2014	0.023%	Most cases culture negative (63.4%) then Coagulase-negative Staphylococci (12.5%)	Diabetes mellitus, older age (mean age of 81 y), rural patients Vitreous loss, ECCE, surgery on left eye
Lundstrom et al, 2015 <sup>15</sup>	Sweden	2002–2010	0.035%	Staphylococci 31%, Enterococci 27%	Age > 85 y, Vitreous loss, nonuse of intracameral antibiotic
Nam et al, 2015 <sup>22</sup>	Korea	2004–2010	0.037%	N/A	Age > 80 y and spring season
Du et al, 2014 <sup>29</sup>	United States	2006–2011	0.088%	N/A	Low socioeconomic status, male gender, age, and use of immunosuppressant
Wu et al, 2014 <sup>30</sup>	China	2001–2012	0.17%	Staphylococcus epidermidis (77% of culture positive cases)	N/A
Friling et al, 2013 <sup>3</sup>	Sweden	2005–2010	0.029%	Enterococci (31%)	Older age (>85 y), nonuse of intracameral cefuroxime, vitreous loss
Keay et al, 2012 <sup>20</sup>	United States	2003–2004	0.111% for 2004 0.133% for 2003	N/A	Age (>85 y), male sex, Native Americans and black patients, less experienced surgeon
Tan et al, 2012 <sup>31</sup>	Singapore	1999–2010	0.042%	Most cases culture negative (42.9%) then Coagulase-negative Staphylococci (14.3%)	Age, male gender, nonuse of intracameral cefazolin
Das et al, 2011 <sup>32</sup>	India	1993–1998	0.13%	Staphylococcus epidermidis (43.2% of culture positive cases)	Ambulatory low socioeconomic urban patients

Note: ECCE: Extracapsular cataract extraction. N/A: Not available.

There was a case series of 17 patients with toxic anterior segment syndrome caused by intracameral cefuroxime,<sup>45</sup> which could be attributed to the improper preparation of the axetil form of the drug.<sup>46</sup> Overall, this method of prophylaxis is safe, and even large doses of cefuroxime are associated only with transient macular edema and no significant adverse reactions.<sup>47</sup> In the case of retinal toxicity, visual loss is reversible.<sup>48</sup>

Intracameral bolus of cefazolin has also been suggested as a useful method of prophylaxis.<sup>31,49</sup> In a systematic review conducted by Kessel et al, the quality of evidence was estimated high to moderate in favor of risk reduction attributed to intracameral use of cefuroxime, cefazolin, and moxifloxacin.<sup>37</sup>

Adding preoperative topical antibiotic to intracameral administration of cefuroxime does not seem to produce an augmented effect in the prevention of endophthalmitis.<sup>50</sup>

### Diagnosis

Endophthalmitis is a clinical diagnosis further supported by paraclinical tests such as culture of obtained vitreous and B-Scan ultrasonography.<sup>51</sup> Even though approximately 30% of cases of post-operative endophthalmitis are culture negative,<sup>52</sup> isolating the causative organism is the mainstay of treatment.<sup>2</sup> This goal is fulfilled by means of aqueous and vitreous sampling as soon as possible, for gram staining, culture, and polymerase chain reaction (PCR) test.<sup>53</sup>

### Management

Intraocular administration of antibiotics is considered the basic fundamental step in the management of endophthalmitis.<sup>54</sup> In order to control massive inflammation caused

by bacterial infection, simultaneous intravitreal injection of unpreserved dexamethasone is advocated.<sup>53</sup> Initially, a broad spectrum combination of antibiotics such as vancomycin and ceftazidime or vancomycin and amikacin are injected intravitreally as first- and second-line therapy, respectively.<sup>55</sup> Amphotericin B, miconazole, and voriconazole are the drugs of choice in the case of fungal endophthalmitis.<sup>56,57</sup> Intraocular injections can be repeated at intervals of 48–72 h based on clinical response.<sup>53,58</sup>

There is not yet a consensus on whether giving systemic antibiotic is beneficial or not. Endophthalmitis vitrectomy study (EVS) found no difference in final visual acuity of patients receiving systemic antibiotics in comparison with those who did not.<sup>59</sup> However, the ESCRS emphasizes administering adjunctive systemic antibiotic therapy for management of acute post operative endophthalmitis.<sup>53</sup>

Immediate complete pars plana vitrectomy is the gold standard of treatment of refractory or fulminate acute post cataract surgery endophthalmitis.<sup>53</sup> Similar to draining an abscess, vitrectomy debrides ocular contents of pus. Obviously, vitrectomy needs an operation room, in contrast to intravitreal injection which can be done in an office setting.<sup>14</sup> Zhang et al believe that silicon oil tamponade is not necessary until occurrence of retinal tear or detachment, and IOL removal is not mandatory primarily.<sup>60</sup> EVS results demonstrate that only patients in a subgroup of initial light perception-only vision or worse derive a benefit from immediate pars plana vitrectomy.<sup>59</sup> However, in cases of rapidly worsening visual acuity or endophthalmitis caused by virulent bacteria, immediate vitrectomy is recommended.<sup>61</sup>

Visual outcome mainly depends on bacteriology and timing of treatment with appropriate approaches. Eighty-four percent of patients with gram positive, coagulase-negative micrococci endophthalmitis achieve visual acuity of 20/100 or better. On the other hand, a positive gram stain infection rather than *Staphylococcus epidermidis* or gram negative cultures are associated with a significantly poorer visual outcome. Presenting visual acuity is also a powerful predictor of final visual outcome.<sup>3,62</sup> In Lundstrom et al's study, communication with vitreous yielded the worst visual outcome.<sup>15</sup>

### Chronic post cataract endophthalmitis

Generally caused by *Propionibacterium acnes*, this entity is an indolent form of endophthalmitis usually presented 6 weeks or more after cataract surgery.<sup>63,64</sup> The patients typically complain of moderate pain and decreased visual acuity. Persistent presence of low level cell and flare in the anterior chamber is the hallmark of the disease.<sup>14</sup> Low-virulence organism being dormant in posterior capsule has been proposed as the causative mechanism for chronic endophthalmitis. Intra vitreal antibiotics, IOL extraction, capsule bag removal, and vitrectomy are treatment options based on clinical course.<sup>65</sup>

### Discussion

American Society of Cataract and Refractive Surgery conducted an online survey from its members in 2014 indicating a growing incline toward the use of intracameral antibiotic compared with a 2007 survey, and the major concern about this method was the low availability of commercially-prepared formulas for intracameral injection.<sup>66</sup>

It seems that in recent years, the hottest topic regarding prophylaxis of endophthalmitis is focused on intraoperative intracameral antibiotic. Relative safe profile and high efficacy of this method is observed in many studies; however, more well-designed randomized clinical trials are needed to confirm the suitability of intracameral antibiotics. Important questions such as the antibiotic type, safety profile, and potential complications should be addressed. Based on current evidence, it seems that intracameral antibiotic at the end of cataract surgery is an effective approach to reduce the risk of endophthalmitis.

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