



Immediate Vitrectomy for Acute Endophthalmitis in Patients with a Visual Acuity of Hand Motion or Better

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Purpose: To determine the efficacy of immediate pars plana vitrectomy as the primary treatment for acute endophthalmitis in patients with a visual acuity (VA) of hand motion (HM) or better.

Methods: A total of 149 patients who were referred to a single center for acute endophthalmitis after cataract surgery over the 13-year study period were retrospectively analyzed. Only patients presenting with a VA of at least HM were included. Patients were initially treated with either primary vitrectomy or intravitreal antibiotic injection alone, and their visual outcomes and reintervention rates after initial treatment were compared.

Results: There was no significant difference in the proportion of good (final VA $\geq 20 / 40$) and poor (VA \leq counting finger) visual outcomes between the groups. However, subgroup analysis of patients with a VA of HM (92 eyes) showed that the incidence of reintervention (14 of 72 eyes [19.4%] vs. 9 of 20 eyes [45.0%]) and poor visual outcomes (10 of 72 eyes [13.9%] vs. 8 of 20 eyes [40.0%]) were lower after prompt vitrectomy than after intravitreal antibiotic injection alone ($p = 0.019$ and $p = 0.022$, respectively). For those with a VA of at least counting finger, no significant difference was observed between the groups.

Conclusions: For patients with endophthalmitis presenting with a VA of HM, performing a prompt vitrectomy reduced the incidence of reintervention and poor visual outcomes than the administration of intravitreal antibiotics alone. Our results suggest that primary vitrectomy for patients with endophthalmitis presenting with a VA of HM could be more beneficial than intravitreal antibiotic injection alone.

Key Words: Cataract; Endophthalmitis; Phacoemulsification; Visual acuity; Vitrectomy

Although infectious endophthalmitis is a rare complication of ocular surgery, it is a severe infection that can affect vision, and requires prompt and effective treatment.

Cataract surgery is one of the most commonly performed surgical procedures globally [1]. The incidence of endophthalmitis after cataract surgery using modern phacoemulsification has been reported to be between 0.02% and 0.08% [2].

Since the mid-1990s, one of the most important studies on the treatment of endophthalmitis has been the Endophthalmitis Vitrectomy Study (EVS). The EVS was a multicenter, randomized, prospective clinical trial that involved 420 consecutive cases of endophthalmitis and was used to

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establish guidelines for the management of infectious endophthalmitis. The study concluded that vitrectomy had no benefit when visual acuity (VA) was better than light perception (LP) [3].

Vitrectomy has been increasingly performed in patients with endophthalmitis presenting with VAs better than LP, although this practice disregards the EVS guidelines [4,5]. According to data from the Medicare database, in the United States, between 2003 and 2004, primary vitrectomy was performed in 41% of endophthalmitis cases with an initial VA better than LP [6]. Another survey from Canada reported that most of the Canadian vitreoretinal surgeons did not strictly follow the EVS guidelines: 56.7% performed primary vitrectomy for patients with endophthalmitis who had a VA of hand motion (HM) instead of treating them with intravitreal antibiotics alone (36.7%) [7]. This trend was likely affected by the remarkable progress in vitrectomy technology since the 2000s, including sutureless small-gauge vitrectomy and the use of a wide-viewing system.

Currently, there is no consensus on the effectiveness of immediate vitrectomy as an initial treatment for endophthalmitis after cataract surgery. It is therefore appropriate to validate the conclusions of the EVS, especially those regarding patients with an initial VA better than LP. The purpose of this study was to determine the efficacy of immediate pars plana vitrectomy as the primary treatment for acute endophthalmitis in patients with a VA better than LP (HM or better).

Materials and Methods

Ethics statement

The study was approved by the Institutional Review Board of Kim's Eye Hospital, Konyang University College of Medicine (No. 2020-02-002), and it conformed to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived by the Institutional Review Board of Kim's Eye Hospital.

Subjects

We retrospectively reviewed computerized medical records and collected the data of patients who were referred

from other local hospitals due to acute endophthalmitis after cataract surgery. All patients were referred from facilities across South Korea and treated at Kim's Eye Hospital, a referral center in South Korea, between January 2007 and December 2019.

Postoperative endophthalmitis was diagnosed by vitreoretinal specialists when decreased VA was combined with the following typical clinical features: marked intraocular inflammation, conjunctival injection, and hypopyon. Toxic anterior segment syndrome was ruled out using ultrasound after confirming significant vitritis at baseline. Only the patients presenting with a VA of HM or better were included in the analysis (those with VAs of LP or worse were excluded). We included all the referred patients with endophthalmitis; however, those with more than 7 days of referral delay were excluded. In addition, patients with endophthalmitis after vitrectomy, bleb complications from glaucoma surgery, penetrating trauma, or intravitreal injection were excluded.

Initial treatment and reintervention

Patients were initially treated with either primary vitrectomy or intravitreal antibiotic injection alone. Those who underwent an initial treatment of intravitreal antibiotics received an intravitreal injection of vancomycin hydrochloride (1.0 mg in 0.1 mL) and ceftazidime (2.25 mg in 0.1 mL). At the discretion of the surgeon, some patients also received an intravitreal injection of dexamethasone sodium phosphate. All injections were performed on the day of diagnosis, without delay, in a sterile surgical room.

When a patient's fundus could not be assessed due to media opacities, immediate vitrectomy was performed as an initial treatment, regardless of the presenting VA. Specific indications for immediate vitrectomy are as follows: (1) severe vitreous opacity (vitritis) confirmed on ultrasound or no red reflex and/or (2) severely edematous cornea. For such patients, pars plana vitrectomies were performed using a standard 23G or 25G transconjunctival vitrectomy system. Vitrectomy was performed to remove as much vitreous as possible, including the induction of posterior vitreous detachment, except in cases of necrotic retina or severe vitreous haziness, where inducing posterior vitreous detachment is difficult. Intravitreal antibiotics were injected at the end of the vitrectomy.

At baseline, the anterior chamber fluids and vitreous

specimens were collected and an antibiotic sensitivity test was performed for each patient. During each vitrectomy, an initial undiluted vitreous specimen was obtained before the fluid infusion was initiated and after all the sclerotomies had been performed. Cultures from the samples were incubated on blood agar, chocolate agar, thioglycolate broth, and fresh Sabouraud dextrose agar.

Twenty-four to 48 hours after the initial procedure, patients were reevaluated for endophthalmitis. Improvement was defined as increased VA, clearer media in the vitreous or anterior chamber, and pain relief. However, if there was no significant improvement at the time of reevaluation, re-interventions, including additional pars plana vitrectomies with intravitreal antibiotic injections, were performed until the vitreous and anterior chambers were sufficiently clear.

Statistical analysis

The final VA was defined as the best-corrected VA after the resolution of intraocular inflammation. The proportion of patients with good visual outcomes (final VA $\geq 20 / 40$) and poor visual outcomes (final VA \leq counting finger [CF]) were compared between the prompt vitrectomy and intravitreal antibiotic injection groups. Further, the rate of re-intervention was compared between the subjects. A subgroup analysis was also performed for the patients who presented with a VA of HM, CF, and better than 5 / 200. Continuous variables were analyzed using a *t*-test, and categorical variables were analyzed using the chi-square test with Yates's correction. All statistical analyses were performed using the commercially available software package PASW SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA), and a *p*-value of <0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 196 eyes of 196 patients were diagnosed with acute endophthalmitis after cataract surgery and treated during the 13-year study period. Forty-seven eyes were excluded because of an initial VA of LP or worse (37 eyes) or a referral delay of more than 7 days (10 eyes). Thus, 149 eyes of 149 patients (70 female and 79 male patients) were eligible for inclusion. The mean age of the patients was

67.5 years (range, 41–84 years) at the time of diagnosis. The mean length of follow-up was 12.4 months (range, 3 months to 8 years; median, 6 months).

The mean time from cataract surgery to the onset of endophthalmitis symptoms was 4.82 days (range, 1–20 days). Endophthalmitis manifested within 3 days in 71 eyes (47.7%), within 4 to 7 days in 51 eyes (34.2%), and after more than 7 days postoperatively in 27 eyes (18.1%). The mean duration from the development of symptoms to referral was 3.14 days (range, 0–7 days). For 102 patients, a referral was made within 3 days, and for 47 patients, it was made within 4–7 days.

The presenting VA was HM in 92 eyes (61.7%), CF in 20 eyes (13.4%), and better than CF (more than 5 / 200) in 37 eyes (24.8%). The baseline characteristics of the patients are summarized in Table 1.

Most of the patients were referred without any intervention after the diagnosis of postoperative endophthalmitis.

Table 1. Baseline characteristics of patients referred due to endophthalmitis after cataract surgery presenting visual acuity of hand motion or better (n = 149)

Characteristic	Value
Age (yr)	67.5 (41–84)
Follow-up period (mon)	12.4 (3–100)
Sex	
Male	79 (53.0)
Female	70 (47.0)
Involved eye	
Right	72 (48.3)
Left	77 (51.7)
Presenting visual acuity	
Hand motion	92 (61.7)
CF	20 (13.4)
Better than CF (more than 5 / 200)*	37 (24.8)
Time from surgery to presentation (day)	
1–3	71 (47.7)
4–7	51 (34.2)
>7	27 (18.1)
Presence of hypopyon at presentation	79 (53.0)
Ruptured posterior capsule at presentation	5 (3.4)
Intraocular pressure at baseline (mmHg)	14.4 (6–38)

Values are presented as mean (range) or number (%).

CF = counting finger.

*Range, 5 / 200 to 20 / 30.

However, 29 of 149 patients (13.4%) had undergone immediate treatment at their local hospital before referral: 28

Table 2. Results of bacterial cultures from patients referred due to endophthalmitis after cataract surgery (n = 85)

Pathogen	No. (%)
Gram-positive bacteria	62 (72.9)
<i>Staphylococcus epidermidis</i>	35 (41.2)
Methicillin-resistant <i>S. epidermidis</i>	1 (1.2)
<i>Streptococcus sanguinis</i>	4 (4.7)
<i>Streptococcus mitis</i>	3 (3.5)
<i>Streptococcus pneumoniae</i>	2 (2.4)
<i>Streptococcus agalactiae</i>	3 (3.5)
<i>Staphylococcus lugdunensis</i>	2 (2.4)
<i>Streptococcus salivarius</i>	2 (2.4)
<i>Enterococcus faecalis</i>	10 (11.8)
Gram-negative bacteria	20 (23.5)
<i>Pseudomonas aeruginosa</i>	13 (15.3)
<i>Acinetobacter baumannii</i>	2 (2.4)
<i>Klebsiella pneumoniae</i>	1 (1.2)
<i>Alcaligenes xylosoxidans</i> subsp. <i>denitrificans</i>	1 (1.2)
<i>Stenotrophomonas maltophilia</i>	3 (3.5)
Fungus	3 (3.5)
<i>Aspergillus</i> sp.	2 (2.4)
<i>Candida</i> sp.	1 (1.2)

patients received intravitreal antibiotic injections and one patient had undergone a partial vitrectomy.

Of the 149 bacterial cultures, 85 (57.0%) were positive and 64 (43.0%) were negative for bacterial growth. Among the positive cultures, 62 (72.9%) were gram-positive bacteria, 20 (23.5%) were gram-negative bacteria, and three (3.5%) had fungal growth. The most commonly isolated gram-positive bacterium was *Staphylococcus epidermidis* (35 eyes), followed by *Enterococcus faecalis* (10 eyes). *Pseudomonas aeruginosa* (13 eyes) was the most common gram-negative bacterium isolated. The culture results are presented in Table 2.

Pattern of initial treatment and visual outcome

Of the 149 cases investigated, primary vitrectomy with intravitreal antibiotic injections was performed in 92 patients (61.7%), and 57 patients (38.3%) received intravitreal antibiotic injection alone. The percentage of patients in the primary vitrectomy group who presented with VAs of HM, CF, and 5 / 200 or better were 78.3% (72 of 92 cases), 45.0% (9 of 20 cases), and 29.7% (11 of 37 cases), respectively.

There was no statistical difference in the proportion of patients with good visual outcomes (final VA $\geq 20 / 40$) after treatment in the primary vitrectomy group (50 of 92 eyes, 54.3%) and intravitreal antibiotic injection alone

Table 3. Proportions of good visual outcomes (more than 20 / 40 final VA) after endophthalmitis treatment in the primary vitrectomy and intravitreal antibiotic injection groups

Initial treatment	Total	Final VA $\geq 20 / 40$	p-value*
Total cases presenting VA of HM or better	149	85 (57.0)	0.523
Primary vitrectomy	92	50 (54.3)	
Intravitreal antibiotics only	57	35 (61.4)	
Cases presenting VA of 5 / 200 or better	37	26 (70.3)	0.421
Primary vitrectomy	11	9 (81.8)	
Intravitreal antibiotics only	26	17 (65.4)	
Cases presenting VA of CF	20	11 (55.0)	0.618
Primary vitrectomy	9	5 (55.6)	
Intravitreal antibiotics only	11	6 (54.5)	
Cases presenting VA of HM	92	48 (52.2)	0.457
Primary vitrectomy	72	36 (50.0)	
Intravitreal antibiotics only	20	12 (60.0)	

Values are number of patients.

VA = visual acuity; HM = hand motion; CF = counting finger.

*Chi-square test.

group (35 of 57 eyes, 61.4%; $p = 0.523$) (Table 3).

In a subgroup analysis of patients with a baseline VA of HM, the proportion of patients with good visual outcomes in the primary vitrectomy group (36 of 72 eyes, 50.0%) and intravitreal antibiotic injection group (12 of 20 eyes, 60.0%) did not differ significantly ($p = 0.457$) (Table 3). In the subgroup analysis of patients who presented with a VA

of CF and 5 / 200 or better, there was no statistically significant difference in the proportion of patients with good visual outcomes between the groups (Table 3).

There was no statistically significant difference in the proportion of patients with poor visual outcomes (final VA \leq CF) between the primary vitrectomy group (11 of 92 eyes, 12.0%) and intravitreal antibiotic injection only group

Table 4. Proportions of poor visual outcomes (less than CF final VA) after endophthalmitis treatment in the primary vitrectomy and intravitreal antibiotic injection groups

Initial treatment	Total	Final VA \leq CF	p -value
Total cases presenting VA of HM or better	149	21 (14.1)	0.418*
Primary vitrectomy	92	11 (12.0)	
Intravitreal antibiotics only	57	10 (17.5)	
Cases presenting VA of 5 / 200 or better	37	2 (5.4)	0.591†
Primary vitrectomy	11	1 (9.1)	
Intravitreal antibiotics only	26	1 (3.8)	
Cases presenting VA of CF	20	1 (5.0)	0.741†
Primary vitrectomy	9	0 (0)	
Intravitreal antibiotics only	11	1 (9.1)	
Cases presenting VA of HM	92	18 (19.6)	0.022*
Primary vitrectomy	72	10 (13.9)	
Intravitreal antibiotics only	20	8 (40.0)	

Values are number of patients.

VA = visual acuity; CF = counting finger; HM = hand motion.

*Chi-square test; †Fisher exact test.

Table 5. Patients with endophthalmitis who required reintervention after initial treatment in the primary vitrectomy and intravitreal antibiotic injection groups

Initial treatment	Total	No. of patients	p -value
Total cases presenting VA of HM or better	149	36 (24.2)	0.039*
Primary vitrectomy	92	17 (18.5)	
Intravitreal antibiotics only	57	19 (33.3)	
Cases presenting VA of 5 / 200 or better	37	9 (24.3)	0.331†
Primary vitrectomy	11	2 (18.2)	
Intravitreal antibiotics only	26	7 (26.9)	
Cases presenting VA of CF	20	4 (20.0)	0.531†
Primary vitrectomy	9	1 (11.1)	
Intravitreal antibiotics only	11	3 (27.3)	
Cases presenting VA of HM	92	23 (25.0)	0.019*
Primary vitrectomy	72	14 (19.4)	
Intravitreal antibiotics only	20	9 (45.0)	

VA = visual acuity; HM = hand motion; CF = counting finger.

*Chi-square test; †Fisher exact test.

(10 of 57 eyes, 17.5%; $p = 0.418$) (Table 4). In addition, there was no statistically significant difference in the incidence of retinal detachment requiring silicone oil tamponade during treatments between the primary vitrectomy group ($p = 0.655$; 4 of 92 eyes, 4.3%) and intravitreal antibiotic injection only group (2 of 57 eyes, 3.5%). However, among the patients with a VA of HM, the proportion of those with poor visual outcomes was significantly higher in the intravitreal antibiotic injection only group (8 of 20 eyes, 40.0%) than in the primary vitrectomy group (10 of 72 eyes, 13.9%; $p = 0.022$) (Table 4).

Reintervention

Thirty-six of 149 eyes (24.2%) of total participants required reintervention for infection control. Reintervention after initial treatment was significantly more frequent in the intravitreal antibiotic injection group than that in the primary vitrectomy group ($p = 0.039$) (Table 5). Specifically, 17 of 92 patients (18.5%) initially treated with primary vitrectomy underwent an additional vitrectomy or intravitreal antibiotic injection, whereas 19 of 57 patients (33.3%) initially treated with intravitreal antibiotic injections underwent reintervention to control inflammation. Additionally, in the subgroup analysis of the 29 patients who underwent intravitreal antibiotic treatment before referral, primary vitrectomy cases (three of 23 cases, 13.0%) showed a significantly lower rate of reintervention than the cases of intravitreal antibiotic injection only (three of six cases, 50.0%; $p = 0.043$).

These results were consistent in the subgroup analysis of patients presenting with a VA of HM, with reintervention being significantly more frequent in the intravitreal antibiotic injection group (9 of 20 eyes, 45.0%) than in the primary vitrectomy group (14 of 72 eyes, 19.4%; $p = 0.019$) (Table 4). However, this difference was not significant among the patients who presented with VAs of CF and 5 / 200 or better (Table 5).

Discussion

Pars plana vitrectomy may have several advantages for the management of endophthalmitis because it allows for a large specimen to be used for diagnostic evaluation, permits the removal of an infectious agent, and enables a re-

duction in the inflammatory debris or mediators in the vitreous cavity [6,8]. Furthermore, there is increased access to the retina with vitrectomy, allowing for easier administration of intravitreal antibiotics [9]. These advantages need to be weighed against the risk of postoperative complications, such as retinal tears and the morbidity associated with undergoing an additional procedure.

The EVS results recommended primary vitrectomy only for patients presenting with a VA of LP or worse because there was no evidence that it improved visual outcomes for those with initial VAs better than LP (HM or better) [3]. In the current study, which did not strictly follow the EVS guidelines, 62.2% of the enrolled patients with initial VAs of HM or better underwent primary vitrectomy. Primary vitrectomy was performed in 76.8% of the patients presenting with a VA of HM, although the administration of an intravitreal antibiotic injection alone is the recommended initial treatment. In the study, prompt vitrectomy for endophthalmitis patients with a VA of HM or better did not improve the chances of a good final VA, which is consistent with the EVS recommendations. However, according to the findings of this study, immediate vitrectomy for endophthalmitis patients with a VA of HM may reduce the risk of reintervention and the proportion of patients with poor visual outcomes after treatment.

Improved surgical techniques and technology may motivate physicians to perform immediate vitrectomy for endophthalmitis rather than strictly follow the EVS guidelines. The small-gauge, wide-angle viewing vitrectomy system, which has been used since the 2000s, is associated with decreased surgical duration, less tissue manipulation, reduced inflammation and postoperative complications, and more rapid visual recovery [10-12]. The definition of a pars plana vitrectomy in the EVS study was the removal of at least 50% of the vitreous. However, with the current advancements in vitrectomy technology, the complete removal of the vitreous may be possible, leading to a lower rate of complications than that reported by the EVS. The complete removal of vitreous to treat endophthalmitis may decrease the need for repeated interventions and shorten the treatment period or recovery time [4,9].

Bacterial virulence is an important prognostic factor in the management of endophthalmitis [13]. The visual outcomes of endophthalmitis cases caused by highly virulent organisms, such as *E. faecalis*, *P. aeruginosa*, *Streptococcus pneumoniae*, or *Klebsiella pneumoniae*, are generally

poor [14]. A higher bacterial virulence could lead to more severe inflammation of the posterior segment and more rapid damage of the retinal tissue [14]. In addition, bacterial virulence varies according to region. For instance, *E. faecalis*, one of the most virulent organisms, is three times more virulent in South Korea than in the United States [9]. However, clinicians may not ascertain the virulence of the infecting strain, and they should treat the endophthalmitis empirically at an early phase. Whether physicians should wait until the VA has deteriorated to LP before vitrectomy (to adhere to the EVS guidelines) has been questionable. Moreover, when vitrectomy is delayed due to VA presentation only, a rapid deterioration of ocular conditions, such as progressive cornea edema, can lead to surgical difficulties stemming from poor visualization and a higher rate of complications. The potential rapid deterioration of ocular conditions caused by highly virulent microorganisms should be considered since clinicians cannot identify and control them at the time of patients' initial presentation. Therefore, an early surgical approach for endophthalmitis deserves more consideration.

In the current study, the patients who were treated with prompt vitrectomy showed significantly less need for reintervention, which allowed for a faster recovery from the infection. Twelve of 23 patients (52.2%) with a baseline VA of HM who received intravitreal antibiotic injections as the initial treatment (as recommended by EVS) eventually required a vitrectomy for infection control. Thus, waiting 24 to 48 hours before performing a vitrectomy after antibiotic injections was not necessary for nearly half of the patients with endophthalmitis who had a VA of HM in this study. A recent report also showed that the need for early reintervention was 54.9% after intravitreal antibiotic injections versus 6.2% after prompt vitrectomy [15]. Lowering the incidence of reintervention may reduce costs and recovery time for patients with endophthalmitis.

Concerning visual outcomes, prompt vitrectomy had no impact on the visual outcomes of patients with VAs of CF or better in this study. A recent investigation regarding acute postoperative endophthalmitis reported similar visual outcomes in the 1st week of presentation between the group treated with intravitreal antibiotics alone and that treated with immediate vitrectomy [16]. In the current study, the proportion of patients with baseline VAs of HM who had poor visual outcomes (final VA \leq CF) was significantly higher in the intravitreal antibiotic injection group

than in the primary vitrectomy group. Our results suggest that immediate vitrectomy for endophthalmitis may be more beneficial than intravitreal antibiotic injections alone for patients presenting with a VA of HM.

To the best of our knowledge, this study included the largest number of patients with endophthalmitis after cataract surgery with initial VAs of HM or better from a single referral center. Moreover, the treatment of endophthalmitis was conducted using a single protocol as much as possible. These are the strengths of this study since endophthalmitis has a very low incidence and is therefore difficult to study.

However, this study also has several limitations, including its retrospective study design. First, delays in treatment before the referral or interventions before the referral may have affected the visual outcomes. The visual outcomes could have been different had the patients been treated at our institution earlier. Second, our study only included cases of endophthalmitis following phacoemulsification. We did not include cases associated with trauma, bleb-related complications following trabeculectomy, vitrectomy, or intravitreal injections to maintain homogeneity of the study population. Given that the prognosis of endophthalmitis varies according to condition [17,18], our results may not be generalizable to all cases of endophthalmitis. Third, Intravitreal dexamethasone or systemic antibiotics were administered at the discretion of the physician. Furthermore, data on systemic antibiotics were unavailable for some patients. However, the role of steroids as adjuvants to intravitreal antibiotics in patients with suspected bacterial endophthalmitis remains unclear [19]. Moreover, the EVS study reported that systemic antibiotics had no effect on visual outcomes [3]. Hence, in our opinion, the administration of dexamethasone or systemic antibiotics would not affect our result. Further investigations on the various presentations of endophthalmitis, including endogenous or chronic endophthalmitis, are warranted.

In conclusion, prompt vitrectomy for patients with endophthalmitis and a VA of HM reduced the incidence of both reintervention and poor visual outcomes. Our results suggest that immediate vitrectomy for patients with endophthalmitis presenting with a VA of HM could be more beneficial than intravitreal antibiotic injection alone. Well-organized prospective randomized studies, which apply the currently improved clinical practice protocols, are encouraged.

Conflicts of Interest: None.

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