Original Article

Treatment Strategies in Acute Post-operative Endophthalmitis after Cataract Surgery at a Tertiary Eye Hospital in Nepal: A 5-year Retrospective Review

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Abstract

Introduction: Despite best possible preventive measures, acute postoperative endophthalmitis (POE) is still the most devastating, sight-threatening complication after intraocular surgery and the most feared complication by treating surgeons.

Materials and methods: It is a retrospective study of 22 eyes diagnosed as acute POE following cataract surgery in the last 5 years (2015-2019), aimed to evaluate the treatment strategies used in its management. Main outcome measures evaluated were rates of repeat intravitreal injection, adjunctive therapeutic regimens, pars plana vitrectomy (PPV) and visual outcome.

Results: 21 eyes (95.45%) received repeated intravitreal injection. Adjuvant intravitreal steroid was used in 12 eyes (54.54%), oral steroid in 16 eyes (72.72%) and oral antibiotic in 8 eyes (36.36%). PPV was done in 8 eyes (34.78%) and all 8 eyes that underwent PPV had a vision of Hand Movement (HM) close to face. 7 eyes (87.5%) had early PPV within 1 week of diagnosis. The median best corrected visual acuity (BCVA) improved from 1.00 logMar to 0.8 logMar following treatment at 3 months follow up (p= 0.117).

Conclusion: Repeat intravitreal injections were commonly employed. Early PPV was performed more commonly regardless of the visual acuity at the time of diagnosis of acute POE.

Key words: Post-operative endophthalmitis, Cataract surgery, EVS, Treatment strategies, Nepal.

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Introduction

Infectious endophthalmitis is a vision-threatening condition that involves inflammation of the entire globe and its intra-ocular contents. The Endophthalmitis Vitrectomy Study (EVS), which was reported in 1995, provided level I evidence in the management of acute postoperative endophthalmitis (POE). The EVS confirmed the benefit of pars plana vitrectomy (PPV) in patients presenting with visual acuity (VA) of light perception (LP) only, in which acute POE occurred within six weeks of cataract extraction or secondary IOL implantation, with no additional benefit over intravitreal antibiotics alone, if vision was hand motion or better. The study also showed that when intravitreal antibiotics were given, systemic antibiotics i.e, intravenous ceftazidime and amikacin, provided no additional visual benefit (Endophthalmitis Vitrectomy Study Group, 1995).

Limitations of the EVS study include the use of traditional vitrectomy equipment and the conservative nature of PPV where induction of posterior vitreous detachment (PVD) and complete vitrectomy were not attempted may have reduced the benefit of vitrectomy surgery. Further, the EVS study did not address the role of intravitreal corticosteroids for endophthalmitis. However, as vitreo-retinal technology has evolved over the years such as due to introduction of wide-angle viewing and transconjunctival 23-27 gauze systems along with newer antibiotics, many ophthalmologists are not following EVS guidelines and are inclined to do early PPV (Gower et al, 2015; Tan C et al, 2008; Almanjoumi AM et al, 2012). However, these data are mostly from the developed and western countries, with limited evidence from Nepal. With this in mind, we evaluated our treatment strategies in acute POE following cataract surgery during the five years period (2014 - 2019).

Materials and methods

This was a retrospective, cross-sectional study. Ethical clearance was obtained from the Nepal Health Research Council (924/2019P) and it also conformed to the provisions of the Declaration of Helsinki 1995.

All patients who presented to the Department of Ophthalmology, Hospital for Children, Eye, ENT and Rehabilitation Services from 1st January 2015 to 31st December 2019, with the diagnosis of acute POE following cataract surgery were included.

Patients were included if they had clinical signs of endophthalmitis within 6 weeks of cataract surgery. POE was diagnosed when patient presented with clinical features, such as pain, blurring of vision, diffuse conjunctival hyperemia, lid swelling, inflammation of the anterior segment (anterior chamber reaction including 1 of the following criteria: flare, cells, hypopyon, fibrin, or cyclitic membrane), and posterior segment inflammation confirmed with ophthalmic ultrasonography. Referred cases of acute POE from other centers who had not received any treatment for endophthalmitis were also included in the study. Exclusion criteria were delayed onset of POE (presenting later than 6 weeks of intraocular surgery), endophthalmitis secondary to surgeries other than cataract or trauma, toxic anterior segment syndrome (TASS), and inadequate data. TASS was excluded when there was pain, absence of limbal to limbal corneal edema and most importantly, vitritis.

A complete record was entered during the initial examination of each patient and included demographic features, complete medical and ocular history, initial ocular examination findings, details of surgery (retrospectively collected from the record files, including any intraoperative complications such as capsular rupture and vitreous loss).

Pre-treatment characteristics for acute POE compared with EVS is given in Table 1.

Once the diagnosis of endophthalmitis was made, informed written consent for the treatment was obtained from the patients after discussing the benefits and the potential risks. The general guideline in its management includes prompt administration of broad-spectrum intravitreal antimicrobials. To mitigate the inflammatory response, some clinicians may add topical or intravitreal steroids during the course of treatment. The role of steroids via any route of administration in endophthalmitis is controversial (Almanjoumi AM et al, 2012). The role of PPV in endophthalmitis, as guided by EVS, was limited in cases whose presenting VA was light perception (LP) (Endophthalmitis Vitrectomy Study Group, 1995).

In our study, the eyes immediately underwent an aqueous and vitreous tap to isolate any organisms, followed by intravitreal injection of antibiotics with or without steroids. . Repeat injection was given when there was no improvement even after 48-72 hours of first injection. Repeat injection was employed either alone or in conjunction with PPV at the close of the surgery. Decision of performing a PPV was left to the discretion of the treating surgeon. However, it was generally performed when there were marked exudates in the vitreous obscuring the view of disc and fundus and those not responding well to intravitreal injection of antibiotics, with or without steroid.

Visual acuity was converted from Snellen to LogMar equivalent during analysis. VA of HM and LP were converted to logMar equivalent, i.e, 2.3 logMar and 2.8 logMar respectively.

Statistical analysis

Mean ± SD and frequency (percentage) were used for continuous and categorical variables respectively. We used median instead of mean for non-normal data. Wilcoxon sign-rank test was used to compare visual acuity LogMar scores before treatment and final visual acuity. Mann-Whitney test was used to calculate mean rank of visual outcome (improvement of VA) among patients treated with vitrectomy versus those treated with only aqueous tap/vitreous tap + intravitreal antibiotics. P-values less than 0.05 were considered statistically significant. All statistical analyses were done by SPSS Version 24, IBM, Armonk, NY, USA.

Results

Demographics

In our study, the commonest age group to be affected was 70-80 years. The mean age of presentation was 68.32 ± 12.99 years. Of these, 50% were males and 50% were females. 5 patients (22.72%) had known diabetes, which were under good glycemic control prior to and following surgery. There was no difference in laterality of the affected eye. None of the patients had blepharitis, meibomian gland dysfunction, ocular surface disorder, nor nasolacrimal duct obstruction prior to the surgery.

Among the acute POE cases, cataract surgeries performed included phacoemulsification (n=20, 91%) and manual small incision cataract surgery (n=2, 9%). The median duration of presentation post cataract surgery was 4.5 days (± 9.81 days, Range 2-42 days). Phacoemulsification surgery was done through suture less, clear corneal incision, and was followed by insertion of an acrylic foldable intraocular lens with the help of an injector. In small incision cataract surgery, cataract was removed through a self- sealing, suture less, scleral tunnel incision made 4 mm behind the superior limbus, followed by insertion of a non-foldable PMMA lens in the bag. As a precaution, 5- 10% povidone-iodine was used for painting periorbital area and was used in cornea and conjunctival sac for a minimum of 3 minutes in all the cases before draping. 0.3 ml of intracameral moxifloxacin (150 mcg/0.1

ml) was given at the end of surgery, through the side port after the main incision was sealed, followed by subconjunctival injection of 0.4 ml of dexamethasone (4 mg/ml) and 0.4 ml of gentamicin (20 mg/ml). No complication was noticed during surgery. None of the cases had used preoperative topical antibiotics, nor did they undergo trimming of eyelashes prior to surgery.

Primary treatment

All 22 infected eyes underwent anterior chamber and vitreous tap at the time of diagnosis. 0.1- 0.2 ml of aqueous was aspirated with a 30 G sterile needle through the limbus, with the patient's eye in primary gaze. The needle was inserted tangentially in a lamellar fashion, keeping its direction oblique over the iris surface and without collapsing the anterior chamber and without inadvertent touch of iris/lens. Similarly, vitreous tap (0.2–0.3 ml approximately) was done via a short 25 to 27 gauge needle on a 3-5 ml syringe at pars plana, avoiding forceful suction, followed by injection of intravitreal antibiotics keeping the needle in situ. Intravitreal antibiotics used in primary and repeat injections were Ceftazidime (2.25 mg/0.1 ml) and Vancomycin (1 mg/0.1 ml). Intravitreal dexamethasone (400 µg/0.1 ml) was given when the suspicion for fungal etiologies was low. Repeat injection was given when there was no improvement even after 48-72 hours, either alone or in conjunction with PPV.

Repeat injection

21 eyes (95.45%) of the eyes received repeated intravitreal injection, either alone or in conjunction with PPV at the close of the surgery. Out of 21 eyes, which 11 eyes (50%) received 3 doses, 10 eyes (45.45%) received 2 doses and 1 eye (4.5%) received a single dose of injection.

Adjuvant therapies used

Out of 22 eyes, adjuvant intravitreal steroid was used in 12 eyes (54.54%), oral steroid was used in 16 eyes (72.72%) and oral antibiotic was used in 8 eyes (36.36%). Oral antibiotic used was Ciprofloxacin 750 mg twice daily for at least 7 days. Patients who received oral steroid were given Prednisolone at a starting dose of 1 mg/kg, within 24–48 h of intravitreal antibiotic administration to lessen intraocular inflammation, and a taper of 60 mg, 40 mg, and then 20 mg, with dose reduction every 3–5 days.

Pars plana Vitrectomy

8 eyes (36.36%) underwent PPV and all 8 eyes that underwent vitrectomy had HM vision at the time of diagnosis. 7 eyes (87.5%) of the eyes had early PPV (within 1 week of diagnosis**).** Out of 11 eyes with HM vision at that time, almost 2/3rd (8 eyes,72.72%) underwent PPV, while 3 eyes (27.28%) did not require vitrectomy as they responded well with 3 doses of intravitreal injections in 2 eyes and 2 doses in 1 eye. None of the eyes underwent primary PPV.

PPV was done using a standard 23 gauge vitrectomy system in all those cases. Specimen of vitreous for microbiological examination was taken from one of the ports prior to turning on the infusion. Induction of posterior vitreous detachment (PVD) was done, if it was not already present. Decision to perform vitreous base shaving was done only in selected cases, depending upon the clinical scenario, where retina did not look necrotic. At the end of surgery, none of the eyes had intravitreal tamponade in the form of oil, gas or air. Intravitreal antibiotics were given at the close of the surgery through one of the ports prior to suturing the port wound.

Visual outcome

Final BCVA following treatment at 3 months was better than the BCVA at the time of diagnosis in 12 eyes (54.54%) and worsened or remained the same in 10 eyes (45.45%) despite

treatment. Even though the median BCVA improved from 1.00 logMar to 0.8 logMar following treatment, it was statistically not significant (p= 0.117). Table 2 demonstrates the distribution of BCVA of the affected eye before cataract surgery, at the time of diagnosis of endophthalmitis and following treatment along with treatment given.

Table 1: Pre-treatment characteristics for acute post-surgical endophthalmitis following cataract surgery compared to EVS

	Our study (n=22)	**EVS (n= 420)**
Mean age	68.32 years± 12.99	-
Sex		
Male	11 (50%)	-
Female	11 (50%)	
Pain	20 (90.9%)	79%
Corneal clarity	12 (54.55%)	*
Hypopyon	6 (27.27%)	75-85%
Media haze obscuring the view of disc and macula	12 (55.55%)	79%

EVS: Endophthalmitis vitrectomy study; *Data not available

Table 2: Distribution of BCVA and treatment given

No	**Age/ Sex**	**Days of presentation**	**BCVA before cataract surgery**	**BCVA at the time of diagnosis**	**Number of intravitreal injections**	**Vitrectomy**	**Adjuvant intravitreal steroid**	**Oral steroid**	**Oral antibiotic**	**Final BCVA at 3 months**
1	65/M	4	6/60	6/6P	2	No	Yes	Yes	No	6/9
2	26/F	2	6/24	6/18	2	No	Yes	Yes	No	6/18
3	70/M	2	CFCF	HM	2	Yes	Yes	Yes	No	1/60
4	73/M	2	6/24P	6/18	2	No	Yes	Yes	No	6/36
5	75/M	7	HM	HM	3	Yes	Yes	Yes	No	HM
6	85/F	5	6/60	6/18	3	No	Yes	Yes	No	6/18
7	65/F	3	1/60	CFCF	3	No	Yes	Yes	No	6/18
8	75/M	2	6/24	1/60	3	No	Yes	Yes	No	6/18
9	81/M	42	2/60	HM	2	No	No	No	Yes	6/18
10	74/F	8	6/36	6/18	1	No	Yes	Yes	No	6/24
11	64/F	7	HM	6/18	3	No	Yes	Yes	No	6/9
12	70/F	4	CFCF	6/18	2	No	Yes	Yes	No	6/18
13	52/M	3	6/36	HM	3	No	Yes	Yes	No	1/60
14	85/M	3	6/12	6/60	3	No	Yes	Yes	No	HM
15	66/M	5	6/18	HM	3	Yes	No	No	Yes	HM
16	58/M	5	3/60	3/60	2	No	No	No	Yes	6/36
17	61/F	4	6/18	HM	2	No	No	Yes	Yes	6/9
18	84/F	5	CFCF	HM	3	Yes	No	No	Yes	6/60
19	72/F	4	6/60	HM	3	Yes	No	No	Yes	HM
20	65/M	14	HM	HM	2	Yes	No	Yes	No	6/60
21	77/F	30	1/60	HM	1	Yes	No	Yes	No	2/60
22	60/F	13	6/60	HM	2	Yes	No	Yes	Yes	6/36

Table 3: Comparison of visual outcome following treatment in various centers in Asia

Study	Year/ Country	VA at the time of diagnosis (% of eyes≥ 20/200)	PPV %	VA at final follow up (% of eyes ≥ 20/200	VA at final follow-up (% of eyes ≥ 20/40)
Our study	2015-2019/ Nepal (n= 22 eyes)	31.81%	36.36%	68.18%	22.27%
Thapa R, et al, 2011	2005-2010 (n=36 eyes)	NA	NA	26.46%	NA
Jung JY, et al, 2008	2001-2006/ South Korea (n=65 eyes)	21.6%	52.3%	77%	49.2%
Choi G J, et al, 1996	1992–2005/ south korea (n= 16 eyes)	0.0%	31.2%	75%	50.0%
Lalitha P, et al, 2008	2002-2003/ India (n= 19 eyes)	21.1%	21.1%	31.6%	26.3%

VA: Visual acuity; PPV: Pars plana vitrectomy

Discussion

In this study, we evaluated the practice pattern for the management of acute POE following cataract surgery, in which we encountered two clusters at different occasions, one in which 13 eyes were affected, the other where 3 eyes were involved and the rest (6 eyes) were sporadic cases. We found that 91% of the eyes that had acute POE were following phacoemulsification, which was higher than in small incision cataract surgery (9%). It may be because phacoemulsification is more commonly performed than small incision cataract surgery. Nevertheless, several retrospective, comparative, case-controlled studies have found a significantly higher POE rate associated with clear corneal incisions compared to sclera tunnel incisions (Cooper BA et al, 2003; Lertsumitkul S et al, 2001; McDonnell PJ et al, 2002; Barrow D et al, 2001). This is thought to be due to postoperative changes in intraocular pressure that may create suction and subsequent inflow of extra-ocular fluid and particles into the anterior chamber (Cooper BA et al, 2003).

We found that 91% of the eyes received repeat intravitreal injection of antibiotics, in marked contrast with EVS, where only 7 % of the eyes received repeat injection (Endophthalmitis Vitrectomy Study Group, 1995). Among the eyes that required repeat injection, half of them required 3 doses (50%), almost half of the eyes received 2 doses (45.45%) and a small proportion received a single dose of injection (4.5%).

Hypopyon was present in 27.27 % of the patients in our study, which is in marked contrast with the findings of EVS (Endophthalmitis Vitrectomy Study Group, 1995) and European Society of Cataract and Refractive Surgeons Endophthalmitis Study (ESCRS), where they reported in 75-85% and 72% of the endophthalmitis patients respectively (Seal D et al, 2008; Seal DV et al, 2006). In our study, fibrinous exudates and marked anterior chamber reaction obscuring the iris and lens details along with vitritis obscuring the view of disc and macula were present in eyes without hypopyon.

Ocular pain was absent in almost one fourth of patients enrolled in the EVS at the time of their initial presentation (Endophthalmitis Vitrectomy Study Group, 1995). But, in our

study, 90.9% of the patients had pain. Likewise, media haze obscuring the view of disc and macula was present in 55.55%, as opposed to 79% in EVS.

Samples obtained from aqueous and vitreous tap were inoculated in blood agar, chocolate agar, Macconkey agar, Sabouraud's dextrose agar and brain heart infusion broth at 37 C. What was surprising in our study, though, was that the vitreous tap specimen on microbiological examination showed gram positive cocci and gram negative bacilli in one case each, but showed no yield on culture plate. This discrepancy could be due to fastidious or non-viable organisms, absence of request for anaerobic cultures, or poor media conditions. Aqueous tap showed no organisms on microbiological examination and culture.

Regarding the treatment, PPV was done in 36.36 % of our patients, which was comparable to other studies (Thapa R et al, 2011; Jung JY et al, 2008; Choi GJ et al, 1996). Among the eyes that had vitrectomy, more than two-thirds (87.5%) had it within a week of surgery. All patients who underwent vitrectomy had a vision of HM close to face. So, we found that vitrectomy was not limited to a vision of LP, which was once an important finding in EVS. Visibility of the disc and macula during examination and poor response to three doses of intravitreal injection was an important deciding factor for PPV in our study.

We also compared the visual outcome following treatment with other studies from Asia (Thapa R et al, 2011; Jung JY et al, 2008; Choi GJ et al, 1996; Lalitha P et al, 2005). Proportion of eyes that attained the final BCVA of logMar 1 (20/200) *versus* (vs) logMar 0.3 (20/40) was 68.18% *vs* 22.27% respectively. Mean ranks of visual outcome (improvement of VA) among patients treated with primary vitrectomy versus only aqueous and vitreous tap + intravitreal antibiotics were 11.70 and 11.07 which is significantly not different (Mann-Whitney U=49.50, n_1=15, n_2=7, P=0.832).

Details of the visual outcome in our study compared with other Asian countries have been depicted in Table 3.

The reasons for no improvement in visual outcome in our study were chronic uveitis (3 eyes), large mutton-fat Keratic precipitates obscuring the clarity (2 eyes), phthisis bulbi (1 eye). The reason for chronic granulomatous inflammation leading to mutton fat keratic precipitates may be similar to that of phacoantigenic uveitis and could be a result of an immune reaction to the presence of both residual lens material and bacteria leading to recurrent and often low-grade uveitis.

Our study has few limitations. Due to the rarity of endophthalmitis, the number of involved eyes was small so as to allow statistical analysis. Other limitations include short follow up and possibility of missing data. As it was a single center retrospective study, its management cannot be generalized. Nevertheless, this study provides useful data on the current management strategies in acute POE. It was designed largely to detect trends that could direct future research. Also, we reported case series that underwent vitrectomy surgery with no control group; so it is not possible to compare our outcomes with a similar cohort of patients with medical management only. So in the future, a randomized clinical trial examining early vitrectomy versus medical treatment alone for acute endophthalmitis is recommended.

Conclusion

The clinical findings and management of acute POE have changed over the years. In our study, marked fibrinous reaction in anterior chamber along with dense vitritis obscuring the view of optic disc and macula**,** in the presence of pain, was a common finding. The treatment strategy used was repeated intravitreal injections and early PPV regardless of the visual acuity at the time of diagnosis of acute POE. This highlights

the need for further multi-center studies in south-east Asia, particularly Nepal to evaluate the current practice pattern and reinforces the need for an updated preferred practice pattern.

Abbreviations:

EVS: Endophthalmitis Vitrectomy Study

POE: postoperative endophthalmitis

PPV: pars plana vitrectomy

BCVA: best corrected visual acuity

VA: Visual acuity

HM: Hand movement

LP: Perception of Light

vs: *versus*

Declarations:

Ethics approval and consent to participate

Written consents were obtained from the patients.

Consent for publication

Written consents were obtained from the patients.

Availability of data and material

The datasets generated and/or analyzed during the current study are not publicly available because the data are strictly confidential, and are the property of the Institution and the Nepal Health Research Council.

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