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ORIGINAL RESEARCH ARTICLE

AN EXPERIENCE OF MANAGEMENT OF CLUSTER ENDOPHTHALMITIS IN WESTERN HILLY RURAL REGION OF NEPAL: A DESCRIPTIVE, INTERVENTIONAL STUDY

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ABSTRACT

Infectious endophthalmitis is among the most serious complications of cataract surgery. Cluster endophthalmitis is defined as five or more cases of endophthalmitis occurring on a particular day in a single operating room in one centre. The study aimed to find out causative organisms, ocular status and visual outcome after an outbreak of cluster endophthalmitis in a high volume cataract surgery in a camp. A descriptive, interventional study was carried out in 18 suspected cases of acute endophthalmitis after manual small incision cataract surgery in a single day. All clinically suspected cases underwent vitreous tap and received intravitreal injections. Vitreous samples were sent for staining and KOH mount, culture, sub-culture and sensitivity test was carried out in all vitreous specimens. Standard treatment protocol was followed. Patients were followed up till six weeks. Of the 89 eyes operated, 18 (20.2%) eyes underwent vitreous tap and intravitreal injections. Mean duration of presentation was 36 hours (24 – 48 hours). Commonest presenting symptom was redness 18 (100%), pain 83.3% (15) followed by decreased vision 77.8% (14). 10 (55.6%) eyes were culture negatives while, 8 (44.4%) were culture positive for pseudomonas aeruginosa. Six (33.3%) eyes needed core vitrectomy and repeat intravitreal injections, whereas 2 (11.1%) eyes needed repeat intravitreal injections only. Eight eyes (44.4%) got a normal visual acuity; two eyes (11.1%) fair and 8 eyes (44.4%) had poor visual acuity according to World Health Organisation (WHO) guidelines. Four eyes (22.2%) needed evisceration, while three (16.7%) eyes progressed to phthisis bulbi. Acute post operative endophthalmitis is a serious complication following cataract surgery. Prognosis of cluster endophthalmitis with proven culture positivity to pseudomonas infection is poor even with prompt standard management.

Key words: *Acute endophthalmitis, Amikacin, Culture sensitivity, Pseudomonas aeroginosa.*

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INTRODUCTION

High volume surgeries in camp set up are common in Nepal, due to the varied topography and geography of the nation; patients are not able to reach the hospital for health care. Eye health care runs parallel to general health system hence, most of the patients in hilly rural regions wait for eye camps or charitable camps for cataract surgeries. These surgical camp can lasts up to 3-5 days depending upon the number of surgeries to be done.

Cataract extraction is the most common intraocular surgery performed worldwide. The evolution of modern cataract surgery has been characterized by a series of remarkable technical refinements. Many of the advances involved changing the type of surgical incision; that is, the transition from intracapsular cataract extraction to extra capsular cataract extraction (ECCE), followed by the transition from ECCE to sutureless manual small-incision

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sclera tunnel cataract surgery, and, the transition of phacoemulsification from sclera tunnel incisions to clear corneal incisions and finally transition from phacoemulsification cataract surgery to use of laser to perform cataract surgeries famously known as femtosecond laser assisted cataract surgery. Manual small incision extra capsular cataract surgery is the most practiced surgery in developing countries. Although technical refinements in the past 2 decades have led to simplified postoperative care and faster visual recovery still, post cataract surgery endophthalmitis has been reported with its incidence of 0.04% to 0.41%.[1-7]

Endophthalmitis occurring within 1 to 14 days postoperatively is classified as acute. The most common cultured organism is Staphylococcus epidermidis, accounting for 60% to 80% of cases.[4] Gram-negative bacteria are responsible for 6% to 29% of cases, however, the rapid progression of infection and their virulence often result in a poor visual outcome despite prompt treatment.[8-10]

Outbreaks of postoperative Pseudomonas aeruginosa endophthalmitis have been described in the literature.[11-19] The association with intrinsic contamination of ophthalmic solutions and contaminated instruments or equipment has been reported.[11-18]

Under aseptic precautions and in sterile operating environment an outbreak of sight threatening or globe threatening post operative cluster endophthalmitis does rarely occur in high volume surgical set up especially in a tertiary hospital. However, same cannot be said when high volume cataract surgeries are performed in camp set up in different conditions. Where even after a proper sterilization of the operation theatre and all the equipments needed for surgery an outbreak cannot be ruled out due to contamination via various sources which cannot be traced number of times.

The purpose of this study is to describe an outbreak of Pseudomonas aeruginosa endophthalmitis after cataract surgery, in a Western hilly rural part of Nepal in a camp set up and outcome after management.

MATERIALS AND METHODS

In the month of October, 2014, 89 eyes of 89 patients had under gone manual small incision extra capsular cataract extraction with polymethyl methacrylate (PMMA) Intraocular lens (IOL), manufactured by Fred Hollows, Kathmandu, Nepal, implantation in a camp set up in Mid-west rural hilly part of Nepal in a single day. Single surgeon operated all the cataract cases with a same surgical team over five hours on the day of surgery.

Diagnosis of endophthalmitis in suspected cases was made primarily on the basis of symptoms of pain, redness, decreased visual acuity, swelling in the eye (Chemosis) and headache and with signs of hypopyon, exudative membrane in the anterior chamber, change in the transparency of cornea and/or vitreous clouding. This was a descriptive, interventional study, where the patients were followed up, up to six weeks after confirming the diagnosis of acute post operative endophthalmitis.

Patients losing follow up, not following standard treatment protocol and not willing to be enrolled in the study were excluded from the study.

The study strictly adhered to the tenets of declaration of Helsinki. An information sheet was provided to all the study participants and an ethical informed consent was taken from the patients. Potential benefits and hazards of the study were described to the patients before enrolling.

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In all endophthalmitis suspected eyes, sub-conjunctival gentamicin 40mgs with dexamethasone 40mgs in 1ml solution was given one dose and atropine 1% eye drops were installed stat. Following which under strict aseptic precautions and local peribulbar anaesthesia, vitreous tap was performed in the isolated minor operation room. A vitreous sample (0.2 to 0.3ml) was obtained by 25 gauze needle aspiration 3.5mm posterior to limbus at supero-temporal pars plana area. Vitreous samples were stained using Grams stain; Giemsa stain and KOH mount in the operation theatre. Intrinsic sources of contamination were also traced and the samples including the operation theatre team's cap, masks, gloves, ringer lactate solution used were separately collected. Both the samples were sent to the hospital's microbiology laboratory for culture and sensitivity testing. With the immediate reports of staining and KOH mount, intravitreal antibiotics and steroid were administered without waiting for culture results. All eyes received intravitreal vancomycin (1000µg in 0.1 ml), amikacin (400 µg in 0.1 ml) and dexamethasone (400 µg in 0.1 ml). Subconjunctival gentamicin 40 mgs (0.5 ml) was given at superior conjunctiva at 12 O'clock area in all cases at the end of the procedure. One drop of atropine eye drop (1%) was instilled before pad bandage. All patients were admitted in isolated ward and were given tablet levofloxacin 750mgs stat and 500mgs twice a day for 7 days along with non steroidal anti inflammatory drugs.

Six hours after the intravitreal injections, topical medications prednisolone acetate 1%, 2 hourly, commercially available milfloxacin 0.5% and gentamicin 1 hourly, cycloplegic (atropine 1%) 8 hourly were given besides giving topical amikacin 5% drops to put six times a day.

Vitreous samples were inoculated in blood agar (aerobic and anaerobic), chocolate agar, and Brain Heart Infusion Media (BHI), all incubated at 37ºC. In addition, room temperature cultures on Sabouraud dextrose agar (SDA) without Cycloheximide were used to grow fungi. Unlike typical fungal cultures,[20] in this study SDA plates were observed in 24 hours and 48 hours and culture reports were correlated with KOH mount findings. A positive culture was defined as growth of the same organism on 2 or more media or had confluent growth on at least one solid medium.

Visual acuity, anterior segment biomicroscopy and fundus examination was done on the next day morning. After 48 hours, eyes with visual acuity of perception of light (PL) only, melting cornea, poor fundal glow, raised intraocular pressure and deteriorating eyes (Photograph 1) were immediately referred to higher centers for further management of possible core vitrectomy and repeat intravitreal injections. The transfer of the patients to higher centers was organized by the charitable organisation and all the patients were accompanied by an Ophthalmic paramedical staff. Remaining patients and their eyes were managed in the base hospital.

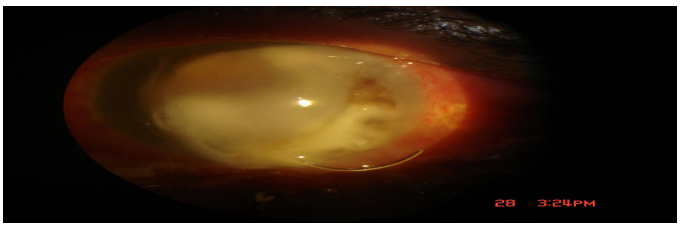

Figure 1: Showing melted cornea with perforated eye with intraocular lens haptic coming out

Referred patients were followed up in tertiary eye hospital with communication through the Ophthalmic assistant accompanying them. Day to day progress report of all the referred cases was kept by the accompanying paramedical staff and the tertiary hospital records.

Remainder of patients were asked to follow up in the base hospital initially every two days for a week then

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weekly and in 4 weeks and 6 weeks time. Referred cases were advised to follow up in first, second, 4 and 6 weeks time. Topical eye drops were tapered according to the patient's ocular status and recovery.

The definitions used in the study were the following

Endophthalmitis: Acute inflammation of the inner layers of the eye ball along with the chambers and cavity.

Uveitis: Inflammation of the eye involving the uveal tissue and mild inflammation of chambers and cavity with good fundal glow.

Pupillary membrane: Grade 4 flare in the anterior chamber and an exudative membrane in the pupil area.

Hypopyon: Pus in the anterior chamber with anterior chamber reaction of 4 plus cells

Standard treatment protocol: Treatment protocol advised by Endophthalmitis Vitrectomy Study (EVS)[8]

Visual acuity: Taken by using standard Snellen's chart and graded using standard classification given by WHO.

Post operative visual acuity WHO guidelines

6/6-6/18	Normal
6/24-6/60	Fair
<6/60	Poor

On each follow up a detailed ocular examination including uncorrected visual acuity and refraction was carried out. Posterior segment was examined carefully. All the data was entered in the profroma made for the study and analyzed using Stastistical Package for Social Services (SPSS) Version 19.

RESULTS

Of the 89 eyes operated, 18 eyes (20.2%) were clinically suspected to have acute post operative endophthalmitis. Mean age of patients was 71.2 years (range: 56-83 years), males 10 (55.6%) eyes were more affected than females 8 (45.4%) gender wise, 11 (61.1%) eyes were right eyes, while 7 eyes (38.9%) were left laterality wise. Mean duration of presentation was 36 hours (range: 24–48 hours). Common presenting features (symptoms and signs) were redness in all 18 (100%) eyes, pain in 15 eyes (83.3%) followed by decreased vision in 14 (77.8%) and anterior chamber reaction (Table 1). 10 eyes (55.6%) were culture negatives and stain negatives, whereas 8 eyes (44.4%) were culture positives and stain negatives with variable sensitivity pattern to various antibiotics tested (Table I). None of the intrinsic source of contamination samples were culture positive or stain positive. None of the culture plates showed mixed growth or contamination. The isolates from eight culture positive plates were same.

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Table I: showing various parameters and findings including clinical features and culture sensitivity

Presenting ocular features and findings on examination in suspected eyes		
Ocular findings (symptoms/signs)	**Number of eyes**	**Percentage (%)**
Redness	18	100
Pain	15	83.3
Decreased visual acuity	14	77.8
Anterior chamber reaction (Cells)	18	100
Hypopyon	2	11.1
Corneal edema	10	55.6
Chemosis	9	50.0
Pupillary exudative membrane	8	44.4
Purulent secretion	8	44.4
Corneal abscess/ulcers	3	16.7
Foreign body sensation	6	33.3
Hyphema	0	0
Shallow anterior chamber	0	0
Soft eye ball	0	0
Increased intraocular pressure	3	16.7
Wound gape	0	0
Vitreous in anterior chamber	0	0
Headache	3	16.7
Fever	0	0
Results of microbiological tests including cultures and sub cultures		
Culture negative vitreous specimen	10	55.6%
Culture positive vitreous specimen	8	44.4%
Sensitivity pattern of culture positive specimens		
Antibiotic tested	**Number of eyes (%)**	**Sensitivity**
Amikacin (§)	8 (44.4)	Partially sensitive (¥)
Gentamicin	8 (44.4)	Resistant
Vancomycin	8 (44.4)	Resistant
Tobramycin	8 (44.4)	Resistant
Cephazoline	8 (44.4)	Resistant
Cefixime	8 (44.4)	Resistant
Ceftriaxone	8 (44.4)	Resistant
Ciprofloxacin	8 (44.4)	Resistant
Milfloxacin	8 (44.4)	Resistant
Levofloxacin	8 (44.4)	Resistant
Penicillin group	8 (44.4)	Resistant

§ = Amikacin was used topically as 5% solution in all the suspected cases before the culture reports came

¥ = All the tested antibiotics were resistant except a partial sensitivity to Amikacin, showing the resistant nature of Pseudomonas aeruginosa isolated from the culture reports, showing similar behavior towards sensitivity to antibiotics.

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Six (33.3%) of 18 cases needed core vitrectomy and repeat intravitreal injections, while two (11.1) eyes needed intravitreal injections only. Preoperative visual acuity in all 18 eyes was less than 3/60; post operative visual acuity in 8 eyes (44.4%) was normal while in 8 eyes (44.4%) it was poor; in two eyes (11.1%) it was fair according to WHO guidelines (Table II) (Photograph 2).

Table II: showing pre-operative visual acuity, visual acuity at the time of diagnosis and visual acuity at last follow up in all suspected acute endophthalmitis cases.

Visual acuity (VA)	Preoperative VA (in eyes) %	Post-operative VA at the time of diagnosis* %	VA at last follow up* (%)
6/6-6/18	0	0	8 (44.4)
6/24-6/60	0	0	2 (11.1)
6/60-3/60	0	10 (55.6)	1 (5.6%)
<3/60-1/60	1 (5.6%)	8 (44.4)	0
<1/60-PL**	17 (94.4%)	0	0
NPL***	0	0	7 (38.9%)
Total	**18 (100)**	**18 (100)**	**18 (100)**

*WHO guidelines for assessment of post-operative visual acuity in cataract surgery cases

**Perception of Light

***No perception of Light

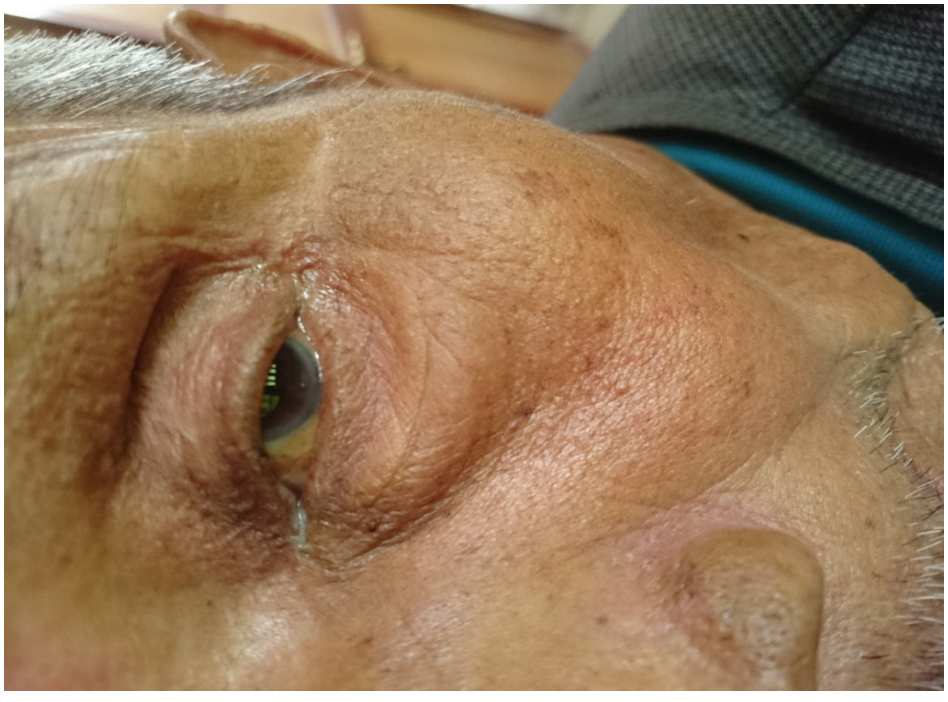

Figure 2: showing a salvaged eye with excellent visual recovery post core vitrectomy and repeat intravitreal injections in four weeks' visit

Of all 18 eyes 11 (61.1%) were salvaged, visual recovery was possible in 11 (61.1%) eyes, however four eyes (22.2%) needed evisceration and three eyes (16.7%) eyes progressed to phthisis bulbi.

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DISCUSSION

The range of endophthalmitis suspect cases turning out to be culture positive is 24 – 85%[21] , which correlated well with the present study (44.4%, 8 eyes culture positive).

Mean age of the patients, mean time of presentation and clinical features of patients at the time of presentation in this study correlated well with the existing knowledge of acute post operative endophthalmitis.[1]

Pseudomonas aeruginosa is one of the most common Gram negative pathogens associated with nosocomial infections.[19] The epidemics seem to be related to contaminated intraocular irrigating solutions.[17-19] Pseudomonas was also identified in povidone-iodine solution.[19] However; in the present study Pseudomonas aeruginosa could not be isolated from any intrinsic source of contamination.

According to the Endophthalmitis Vitrectomy Study (EVS),[8] the recommended treatment for endophthalmitis is primary vitrectomy only for cases with perception of light (PL), any acuity better than this should be submitted to intravitreous antibiotic injection after intraocular fluid aspiration for culture.[8] Chen et al.,[22] suggested that vitrectomy (primary or secondary) reduces the likelihood of sight and globe threatening complications in cases of suspected endophthalmitis at first presentation.[22] However; in the current study none of the patients underwent primary vitrectomy at presentation.

In the present study six out of 18 eyes (33.3%) needed a secondary vitrectomy and two eyes (11.1%) needed repeat intravitreal injections. The EVS protocol was followed in this outbreak, which salvaged 11 (61.1%) eyes with excellent final visual outcome. However on the other hand, even after following the EVS protocol,[8] four eyes (22.2%) needed evisceration during treatment and three (16.7%) improving eyes progressed in to phthisis bulbi in last follow up.

In a study done elsewhere a more aggressive treatment protocol was approached where, primary vitrectomy, vitreous tap and intravitreal injections were given at first presentation in 45 eyes, and repeat secondary vitrectomy with intravitreal injections if needed only. In that study none of the eyes (45 of them) needed evisceration or enucleation; all the eyes were salvaged with good visual outcome.[23] Similarly, in a retrospective study by Charles et al.,[24] in which they analyzed visual outcomes for pseudomonas endophthalmitis, 18 (64%) of 28 eyes were either eviscerated or enucleated. In other study elsewhere, results of pseudomonas endophthalmitis outbreak after cataract surgery were poor as reported by Arsan et al .[25] and only one patient out of four retained visual acuity of 6/60 or better.

Present study had better outcomes after treatment, than the findings of the studies of Charles and Arsan et al.[24,25] However, this study lagged behind with other study[23] in terms of eyes and sight restoration. The comparisons with other studies[23-25] could raise a possible suggestion of aggressive approach for suspected endophthalmitis with primary vitrectomy, vitreous tap and intravitreal injections in first presentation only. But, in a country like Nepal with limited infrastructure especially in remote hilly region with lack of skilled man power EVS treatment protocol[8] still remains gold standard.

Generally the visual prognosis is poor in Pseudomonas endophthalmitis despite of the treatment with intravitreal antibiotics even in cases in which the isolates were sensitive or partially sensitive. In a nine patient reported outcome, five of them reached final acuity of no perception of light (NPL) and no patient

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reached acuity better then 20/400 (6/120).[23] In the EVS, four of the four hundred and twenty patients had confirmed Pseudomonas endophthalmitis and, three of these, had final acuity worse then 20/400 (6/120).[8]

In the present study, high index of suspicion, prompt aggressive available treatment, early isolation of organism, continuous follow up and early referral probably resulted in better visual outcomes in 11 (61.1%) eyes, which differed when compared to the other studies.[23,8]

The choice of antibiotics for injection at the first moment, prior to culture results, aims to cover gram positive and gram negative bacteria. The safety and effectiveness of vancomycin and ceftazidime or amikacin combined has been reported in experimental studies using mice and confirmed in humans in case series.[26] To treat ocular Pseudomonas infection we must take into consideration the increasing prevalence of antibiotic-resistant isolates. Reviewing the literature we have found reports of resistance to various antibiotics as cephazolin, ampicillin, cephalothin, neomycin, chloramphenicol, tetracycline, aminoglycosides, and fluoroquinolones.[23] In the current study, resistance to ampicillin, ampicillin-sulbactam, cephazolin, gentamicin, tobramycin, ciprofloxacin, levofloxacin, milfloxacin, vancomycin, ceftriaxone, cefixime was observed (Table I).

The other antibiotics tested amikacin was partially sensitive to all the Pseudomonas isolates; however ceftazidime was not tested for and was not used for intravitreal injections or topical medications. This finding clearly showed, Pseudomonas isolates are resistant to number of different antibiotics, hence culture sensitivity with variety of antibiotics is needed during management.

Similar studies from other parts of Nepal or reports from elsewhere will elaborate more about Pseudomonas endophthalmitis post cataract surgery. Larger scale data is needed to explore about the resistant pattern of Pseudomonas aeruginosa to various antibiotics as well as the sensitivity pattern, so that a more pin point treatment protocol can be formulated. This study can be a baseline study in upcoming days to provide various features of Pseudomonas endophthalmitis and its management.

CONCLUSIONS/RECOMMENDATIONS

Acute post operative endophthalmitis is a serious complication following cataract surgery. Immediate, prompt intervention involving dedicated team can salvage the eyes and restore better visual outcome. Prognosis of cluster endophthalmitis with proven culture positivity to pseudomonas infection is poor even with prompt standard management.

It might be a better idea especially in tertiary eye hospitals to go for primary vitrectomy, vitreous tap and intravitreal injections in suspected endophthalmitis cases before the culture sensitivity reports come in. However, in a primary or secondary eye hospital or in difficult set ups like camp; Endophthalmitis Vitrectomy Study (EVS) protocol for management can salvage eyes and restore vision. Comparative studies regarding these two management protocols can sustain the hypothesis.

Even with all the safety cataract surgery has achieved, today, endophthalmitis remains a risk and a fearful complication of the procedure. The proper cleaning and sterilization of surgical instruments, surgical quality inputs, and correct prophylaxis are crucial to prevention. In the present study, it was impossible to identify the source of the outbreak.

High level of preservation of eyes and sight in this study was attributable to the dedicated Ophthalmic

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team who were involved in managing cases.

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