ORIGINAL ARTICLE

Management of Post-Operative Endophthalmitis with Intravitreal Vancomycin and Amikacin

Mahmoud A. Salim[1], Babiker Haga Abukheir[2]

1. Assistant Professor, Department of Ophthalmology, University of Gezira.
2. MD. U K, Fellowship of Vitreoretinal Surgery Hyderabad – India, Vitro-Retinal Surgeon Omdurman Military Hospital.

Abstract:

Aims: To assess the outcome of management of post-operative endophthalmitis with intravitreal injections of Vancomycin and Amikacin; both by measuring the visual acuity and assessing the corneal transparency. The study also aimed at identifying the causative organism, by culture and sensitivity and Gimsa staining of the vitreal tap. **Materials and methods:** This study was conducted in Makkah eye complex, Khartoum – Sudan, over a period from April 2003 till December 2004. Patients reported at out patient department(OPD) with signs and symptoms of endophthalmitis within six weeks after cataract surgery, they were examined initially for the visual acuity; then diffuse illumination and bio-microscopy examination was performed for grading clarity of cornea, and for checking presence of hypopyon or sufficient clouding of the anterior chamber, also intraocular inflammation was measured by the assessment of flare, cells, and inflammation membrane. Indirect ophthalmoscopy was performed to examine the red fundal glow and the status of the vitreous and retina. Inside the operating room vitreous and aqueous tap were done for the culture and sensitivity. Then the patients were treated with intravitreal and subconjuctival injection of Amikacin and Vancomycin. **Results:** In a total of (25) patients, pain and blurring of vision were found to be the most common symptoms, Insufficient corneal clarity 23 (92%) of patients, hypopyon was found at different levels in all patients, Red reflex was absent in 21 (84%) of patients. All the patients were found to have either vitritis, choroiditis or both in A and B scan. Post treatment findings of the 19 (76%) patients who attended the final six-month follow-up were as follow: The pain was relieved in all patients. The visual acuity had improved to a maximum of 6/18 one (5%) patient, 2 (10.5%) patients went into phthisis bulbi. The clarity of cornea was observed in 17 (89.5%) patients. Hypopyon disappeared from 17 (89.5%) of patients after injection. Fundal glow reappeared in 12 (63%) of patients. The

results of remaining 6 (24%) patients who attended less than three-month follow-up period were as follow: Pain was relieved in (5) 83% of patients. The visual acuity reached a maximum of 3/60 in (1) 16.7% of patients, (1) 16.7% of the patients went into phthisis bulbi. The clarity of cornea was observed in (5) 83% of patients. (3)50% of patients were having no hypopyon after injection, fundal glow remains absent. Cultures were negative in (15) 60% of cases. (10) 40% showed confirmed growth of different organisms. *Staphylococcus aureus* (1) 4%, S. viridance (1) 4%, *S. epidermidis* (2) 8%, *S. pyogenes* (3) 12% and *S. albus* (3) 12%.

Key words: bacterial endophthalmitis, intravitreal Amikacin and Vancomycin, vitreal tap

Introduction:

Post-operative endophthalmitis is a serious intra-ocular infection that occurs most commonly as a complication of intra-ocular surgery and causes severe visual impairment or the loss of an eye[1,2] As cataract extraction is the most common intra-ocular operation, most cases of endophthalmitis follow cataract surgery. Although the reported rate of post-operative endophthalmitis is low, the prevalence of endophthalmitis has increased significantly with the increasing number of cataract procedures performed. During the last 30 years there have been significant changes in surgical practices for cataract extraction. Intracapsular extraction was the main method used until the late 1970s; extracapsular extraction became the preferred method in the early 1980s due to the introduction of intraocular lens implantation; and improved instrumentation has led to the predominant use of small incision phacoemulsification since the late 1980s. The current state of the art is sutureless phacoemulsification surgery with injected foldable intra-ocular lenses, although some have described a fall in the incidence rate of post-operative endophthalmitis following extracapsular cataract surgery [3, 4].While concerns about an increased risk of endophthalmitis with phaco-emulsification surgery were raised, they have yet to be convincingly demonstrated [5] as phaco-emulsification surgery is almost universally performed today. The lack of information regarding the risk of post-surgical endophthalmitis is a significant gap in our knowledge of the safety of this new method of surgery. Most existing analyses of post- operative endophthalmitis have utilized data derived from individual centers or groups of surgeons which resulted in very low case numbers, making comparisons and statistical validity of data difficult. [3-4]The rarity of the disease means that a randomized control trial is not the appropriate

methodology to study this adverse outcome.Certain risk factors for the development of postoperative endophthalmitis have been suggested. These include cases complicated by inadvertent communication with the vitreous cavity, wound complications such as leaks, as well as surgeries that required prolonged operating time and excessive introduction and reintroduction of instruments into the anterior chamber[6]. The use of intraocular lenses with prolenehaptics appears to increase the chance of endophthalmitis when compared to the haptics made of polymethylmethacrylate (PMMA) [(7)].

Past five decades have rendered cataract a treatable condition in many cases. Post cataract cases are restored to 20/40 acuity or better in approximately 50% of cases in the most favorable subgroups (least virulent organisms, good initial visual acuity, acute onset) but the remainders suffer permanent visual loss to varying degrees. Furthermore, certain sub groups (eg. Streptococcus) have been extremely difficult to treat, apparently due to the inability to control severe post infection inflammation within the eye. Practical strategies involving the use of diagnostic cultures, intravitreal and systemic antibiotic and anti-inflammatory drugs and vitrectomy are presented for both initial management as well as subsequent management of cases that deteriorates[(8)].

Literature review:

Endophthalmitis refers to an infection in which all the coats of the eye are involved. The infectious process, depending on the underlying cause, may present in different manners. If the infectious nidus is internal and has spread from another infected organ, it is called endogenous. If the infectious process follows intraocular surgery or penetrating ocular trauma, it is called exogenous. Both forms of endophthalmitis are true ophthalmic emergencies that can lead to blindness if not diagnosed and treated appropriately and aggressively [(9)].

Infectious endophthalmitis is classified by the events leading to the infection and by the timing of the clinical diagnosis [(10, 11)]. The broad categories include postoperative endophthalmitis (acute, delayed-onset, conjunctival filtering bleb associated), post-traumatic endophthalmitis, and endogenous endophthalmitis. These categories are important in predicting the causative organisms and guiding therapeutic decisions before microbiologic confirmation of the clinical diagnosis.

Bacterial endophthalmitis occurs in a number of clinical settings. Compilation of large reported series suggests the following distribution of cases: 62 percent occur

following intraocular surgery, 20 percent occur following penetrating trauma, 10 percent occur following planned or inadvertent filtering blebs and 8 percent occur as a result of metastatic infection [12, 13, and 14].

The accurate diagnosis of endophthalmitis after cataract surgery requires attention to clinical symptoms and signs, as well as appropriately selected laboratory tests. The earliest symptom of endophthalmitis is usually discomfort or deep pain, although the rapid postoperative improvement in visual acuity with intra ocular lens(IOL) implantation has increased the number of patients reporting a loss of vision as the initial symptom of endophthalmitis. Signs of endophthalmitis include conjunctival hyperemia, chemosis, cells and flare in the anterior chamber, hypopyon, membrane formation on the IOL, vitritis, scattered retinal hemorrhages, loss of red reflex, and in extreme cases, corneal opacification. Retinal periphlebitis may be observed as an early sign of bacterial endophthalmitis [15].

Approximately 64 percent of eyes with a clinical diagnosis of infectious endophthalmitis will have a positive culture result [16, 17].

A major turning point in the development of successful therapy for endophthalmitis occurred in 1944 when Von Sallmann and colleagues demonstrated that the intraocular injection of penicillin eradicated S. aureus endophthalmitis in the rabbit. Intravitreal antibiotic therapy was subsequently developed further and has dramatically improved the possibility of salvaging vision in endophthalmitis [18]. Of all available antimicrobial agents evaluated for intraocular injection, only a few are used regularly in clinical practice. Intraocular vancomycin (1 mg) in combination with an aminoglycoside (amikacin, 0.4 mg, or gentamicin, 0.1 mg) has been a commonly used regimen for the initial empiric treatment of presumed bacterial endophthalmitis [19, 20]. An alternative to the aminoglycosides for coverage of gram-negative organism is the use of intraocular ceftazidime (2.25 mg), a third-generation cephalosporin [21, 22]. Vancomycin has replaced cefazolin (a first-generation cephalosporin) for gram-positive bacterial coverage in recent years because of an increased incidence of coagulase-negative staphylococci resistance to methicillin or other β-lactam antibiotics [23, 24]. Repeated injections of intraocular antibiotics may cause significant retinal toxicity. In view of the low rate of persistent infection after initial combination therapy, repeat injection of intraocular antibiotics should be considered only in those cases with progressive disease caused by virulent organism [25].

Justification:

Postoperative endophthalmitis results from an intraocular infection and usually occurs following cataract surgery. Outcome for the patients can be devastating. Therefore, there is much interest in minimizing the occurrence of endophthalmitis. Modern management, which has included the use of intravitreal antibiotics, has changed the picture. The current treatment approaches can yield excellent visual results in postoperative endophthalmitis.

The purpose of study is to give the outcome of timely management.

Objectives:

1. To assess the outcome of management of postoperative endophthalmitis with intravitrealVancomycin and Amikacin by measuring visual acuity and assessing corneal transparency.
2. To identify the causative organism, by culture and sensitivity and Gimsa staining using vitreal tap.
3. To establish base line data for further study in the same subject.

Materials and Methods:

Study area:

This study was conducted in Makkah eye complex. Khartoum, Sudan. It is one of the biggest ophthalmic centers in Sudan. The study was carried out during period of April 2003 till December 2004.

Study Population:

Patients reported to out-patient department (OPD) of Makkah Eye Complex with signs and symptoms of endophthalmitis within six weeks after cataract surgery from different centers of Sudan.

Methodology:

A questionnaire was designed and completed for each patient. It consisted of:

Bio data, present complaints, history of present complaints, past ocular history, Medical history.

Examination: Visual acuity, Diffuse Illumination, Bio microscopy, Ophthalmoscopy (Direct/ Indirect), Schiotz tonometer. Investigations: A and B SCAN (pre and post treatment), Culture and sensitivity. Smear of aqueous and vitreous for microscopic examination

Study design:

Prospective Study, patients who were eligible for study were examined; only those fulfilling the inclusive criteria, out of the total patients attending out- patient department in Makkah Eye Complex. Bio data which included name, age, and sex were filled in questionnaire.

In the initial examination, vision was tested for the ability to see the Snelen's E chart, if failed then vision was tested for the ability to count fingers, if failed then tested for the ability to recognize hand motions and perception of light. During visual acuity testing the normal eye of the patient was occluded. Diffuse illumination: In addition to examination of ocular adnexa patients were also examined for the sufficient clarity of cornea and anterior chamber to allow the visualization of at least part of iris, and presence of hypopyon or sufficient clouding of the anterior chamber. Biomicroscopy: Patients were examined for cornea to assess corneal edema, and visualization of iris to assess the clarity of cornea. Intraocular inflammation was measured by the assessment of flare, cells, and inflammatory membranes. Size of the hypopyon in mm, inflammation of iris, wound leak, necrotic wound margins, suture abscess were also assessed. Ophthalmoscopy (Indirect): Indirect ophthalmoscopy was performed to see the red fundal glow and the status of the vitreous and retina. Visual acuity and clarity of ocular media are the two most important clinical criteria used for the assessment of treatment outcome. After examination patients were sent to the operation theatre where vitreous and aqueous tap were done for the culture and sensitivity. The samples were cultured in blood agar or in chocolate agar at the same time taps were collected on a glass slide for staining and were sent to the laboratory for results. After collection of the sample patients were treated with intravitreal and subconjunctival injection of amikacin and vancomycin.

Procedure: Tools:

Lid retractor, Caliber, 1 cc syringes: 05Qty, 5 cc syringes: 02Qty, 10 cc syringes: 02 Qty, Two headed sterile swab: 02 Qty.

The patient was given retrobulbar and facial anesthesia preoperatively. Lid retractor was used to separate the lid and to increase palpebral fissure working area. The caliber was used to determine the working distance from the limbus (3.5 mm diagonally). A 25 gauge needle was used for the vitreous tap and 1cc syringe needle was used to aspirate the aqueous sample and both intravitreal and subconjunctival delivery of antibiotics used.

Amikacin was prepared by using 0.1 ml from vial and adding to it 6.15 ml of normal saline so as to get 0.1 ml (which contains 0.4 mg) for intravitreal injection. The subconjunctival volume was 0.1 ml (which contains 25mg) taken directly from the vial and injected.

Vancomycin was prepared first by diluting a 500 mg vial powder with 10ml distilled water then taken from this initial diluents 0.2 ml and adding to it 0.8 ml normal saline to get 0.1 ml (which contain 1 mg) for intravitreal injection. Make partial – thickness sclerotomy 3.5 – 4.0 mm behind limbus. The subconjunctival was 0.5 ml (which contains 25 mg) taken direct from the initial diluents and injected.

Samples for culture (Aqueous and Vitreous) were put in the blood or chocolate agar and with a zigzag movement were spread with a sterile swab. The Petri dishes were rapped with sticker to avoid contamination. The slide sample (Aqueous and Vitreous) was left on the glass slide to dry in room temperature.

Patients were given a date for follow – up next day. During this period results were collected from the laboratory. After one- week patients were examined and assessed for the clarity of cornea (on defined rules) and visual acuity. A and B scan was also done and compared with pre – treatment. Treatment was modified according to the results of culture and sensitivity.

Data analysis:

Data was filled in SPSS (Statistical Package for Social Sciences) program and was analyzed and compared.

Limitation of the Study: Some patients were not attending the follow up on given dates.

Results:

A total of 25 patients: (14) 56% were males, (11) 44% were females included in the study, out of these (19) 76% attended the six months final follow-up, while (6) 24% attended less than three months follow-up. All the patients presented with clinical signs of bacterial endophthalmitis within six weeks of cataract surgery.

The most common symptoms (Table 1)were pain and blurring of vision, visual acuity ranging from 3/60 down till NPL. Insufficient corneal clarity (23) 92% of patients, hypopyon was found at different levels in all patients, Red reflex was absent in (21) 84% of patients. All the patients were found to have vitritis, choroiditis or both in A and B scan.

Table (1): Follow-up-6 months-symptoms.(n=19)

SYMPTOMS		AFTER ENDOPHTHALMITIS		AFTER INJECTION	
		Frequency	Percent	Frequency	Percent
Pain	Yes	19	100.0	1	5.2
	No	-	-	18	94.7
Redness	Yes	19	100.0	1	5.2
	No	0	0	18	94.7
Lid swelling	Yes	19	100.0	2	10.5
	No	0	0	17	89.5
conjunctival chemosis	Yes	19	100.0	2	10.5
	No	0	0	17	89.5
Flare	Unknown	0	0	2	10.5
	Yes	19	100.0	0	0
	No	0	0	17	89.5

Table (2): Follow-up-6 months-signs.(n=19)

SIGNS		AFTER ENDOPHTHALMITIS		AFTER INJECTION	
		Frequency	Percent	Frequency	Percent
cells	Unknown	-	-	2	10.5
	Yes	19	100.0	0	0
	No	-	-	17	89.5
iritis	Clear	1	5.2	16	84.2
	Muddy	18	94.7	1	5.2
	Cannot be recorded	-	-	2	10.5
pupillary membrane	Yes	7	36.8	3	15.8
	No	12	63.2	14	73.7
	Not-recorded	-	-	2	10.5

Post treatment findings of the (19) 76% patients who attended the final six-month follow-up were as follows(Table2):

The pain was relieved in all patients. The visual acuity had improved to a maximum of 6/18 (1) 5% patient, (2) 10.5% patients went into phthisis bulbi. The clarity of cornea was observed in (17) 89.5% patients.

Hypopyon disappeared from (17) 89.5% of patients after injection. Fundal glow reappeared in (12) 63% of patients (Table 3).

The results of remaining (6) 24% patients who attended less than three-month follow-up period were as follow: Pain was relieved in (5) 83% of patients. The visual acuity reached a maximum of 3/60 in (1) 16.7% of patients, (1) 16.7% of the patients went into phthisis bulbi (Table 4). The clarity of corneal was observed in (5) 83% of patients. (3) 50% of patients were having no hypopyon after injection, fundal glow remains absent (Table 5).

Cultures were negative in (15) 60% of cases. (10) 40% showed confirmed growth of different organisms. *Staphylococcus aureus* (1) 4%, *S. viridance* (1) 4%, *S. epidermidis* (2) 8%, *S. pyogenes* (3) 12% and *S. albus* (3) 12%.

Table (3): Follow-up-6 months-investigation results.(n=19)

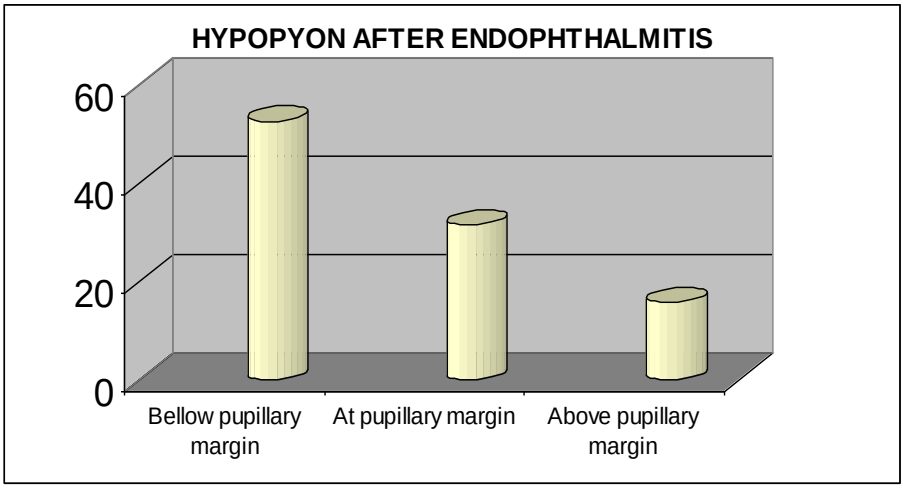
INVESTIGATION		**AFTER ENDOPHTHALMITIS**		**AFTER INJECTION**	
		Frequency	**Percent**	**Frequency**	**Percent**
fundal glow	Yes	4	21.0	12	63.2
	No	15	78.9	5	26.3
	Not recorded	-	-	2	10.5
intraocular pressure	High	6	31.6	0	0
	Normal	13	68.4	16	84.2
	Low	0	0	1	5.2
	Not-recorded (Soft)	0	0	2	10.5

Table (4): Follow-up-3 months-symptoms and signs.(n=19)

SYMPTOMS AND SIGNS		AFTER ENDOPHTHALMITIS		AFTER INJECTION	
		Frequency	Percent	Frequency	Percent
pain	Yes	6	100.0	1	16.7
redness	Yes	6	100.0	2	33.3
lid swelling	Yes	6	100.0	1	16.7
conjunctival chemosis	Yes	6	100.0	2	33.3
flare	Unknown	0	0	1	16.7
	Yes	6	100.0	1	16.7
	No	0	0	4	66.7
cells	Unknown	0	0	1	16.7
	Yes	6	100.0	1	16.7
	No	0	0	4	66.7
iritis	Muddy	6	100.0	5	83.3
	Cannot be recorded	-	-	1	16.7

Table (5): Follow-up-3- investigation results.(n=19)

INVESTIGATION RESULTS		AFTER ENDOPHTHALMITIS		AFTER INJECTION	
		Frequency	Percent	Frequency	Percent
fundal glow	No	6	100.0	5	83.3
	Not recorded	0	0	1	16.7
pupillary membrane	Yes	5	83.3	3	50.0
	No	1	16.7	2	33.3
	Not recorded	0	0	1	16.7
intraocular pressure	Normal	1	16.7	3	50.0
	High	5	83.3	2	33.3
	Can not Be recorded	-	-	1	16.7



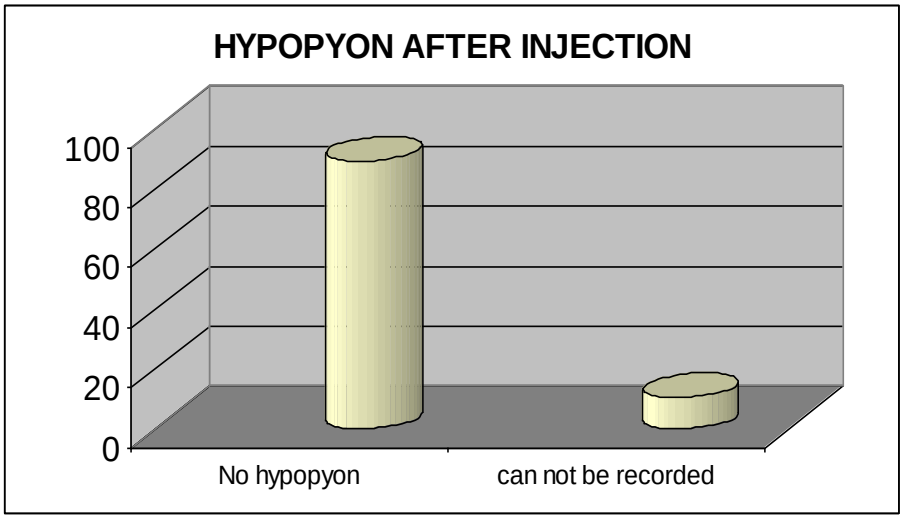
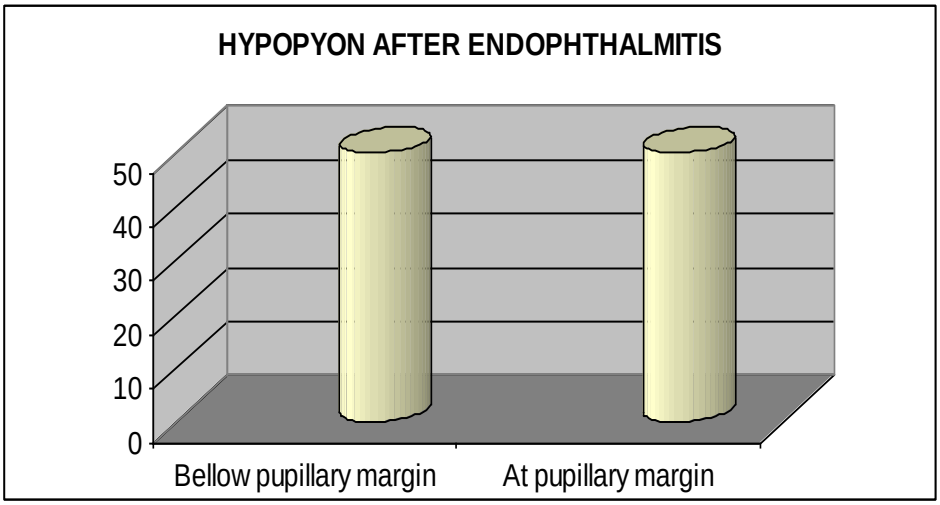


Figure (1) and (2): for the 19 patients



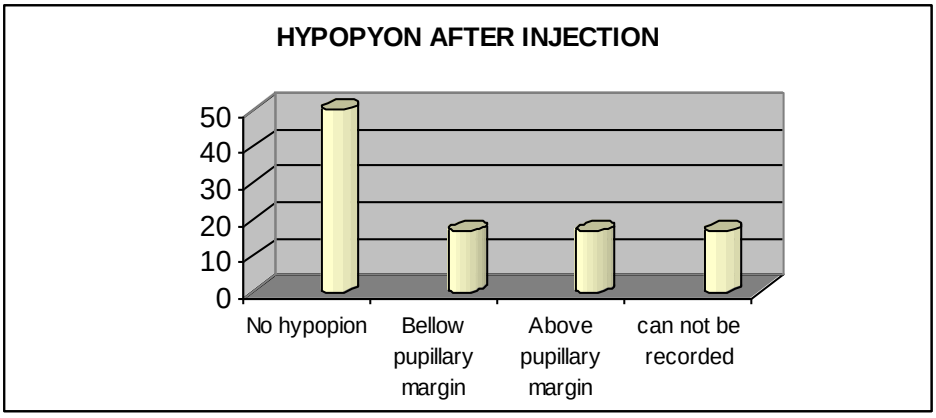


Figure (3) and (4): for the 6 patients

Conclusions:

Endophthalmitis after cataract extraction with severe visual loss have no too distant past. Modern management with the use of antibiotics like povine iodine 5% preoperatively and an intravitreal antibiotics postoperatively, has changed the picture. Preoperatively assessments are very important to prevent the endophthalmitis. Abnormalities and infections of adnexis, conjunctiva and cornea should be treated preoperatively. It has been observed that the patient's hygienic conditions are often the source of the organism causing infections.

Constant attention to postoperative complains of patients is critical, since early diagnosis allows early intervention and better outcomes.

The mainstay of management is immediate introduction of intravitreal drugs that cover both gram positive and gram negative organism. Although the most common organisms that cause endophthalmitis are gram positive, at presentation it is very difficult to confirm the organism type, so intravitreal antibiotics to cover both organisms are used.Intravitreal antibiotics were given to all patients of the study, and those included either patients from perception of light (PL) or more hand motion (HM),counting fingers (CF) or more.In all patients an improvement in pain, the signs of inflammation and general condition of the patient was observed. Hand motion visual acuity patients got advantage that most of them had an improvement in their visual acuity sometimes up to 6/18. In perception of light visual acuity patients, though the visual improvement was not remarkable, they end up saving their globe (in the term of pthisisbulbi) resulting in a lesser psychological trauma than being eviscerated.

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