

Visual acuity outcomes after intra vitreal ceftazidime in acute post-operative endophthalmitis

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ABSTRACT

Objective: To determine effectiveness of ceftazidime as an intraocular antibiotic in the treatment of acute post operative endophthalmitis.

Methodology: This was an observational clinical analysis conducted on patients presenting with acute post-operative endophthalmitis. The study was conducted at Liaquat University Eye Hospital of Liaquat University of Medical and Health Sciences /Jamshoro, Pakistan. Both culture positive and negative subjects were enrolled. Anterior segment slit lamp examination and if possible posterior segment examination was performed. After completing emergency investigations, vitreous tap was carried out followed by intravitreal injection of ceftazidime (2.25%) through pars plana approach. The post-resolution best corrected visual acuity was recorded.

Result: Out of thirty four subjects, 32.4% (11 Eyes) showed good response with post treatment visual acuity of 6/24 and better. 41.2% (14) eyes had moderate improvement with visual outcome of 6/60 and better. Intravitreal injection ceftazidime was repeated on nine subjects after forty eight hours of first injection. Four (11.7%) patients out of nine with repeat injection improved to 6/60 and better, and five (14.7%) with poor response were referred to vitreo retina department.

Conclusion: Ceftazidime has proved to be quite effective in acute post operative endophthalmitis caused by both gram positive and gram negative organisms.

KEY WORDS: Acute endophthalmitis; Intra ocular surgery; Intra vitreal ceftazidime.

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INTRODUCTION

Endophthalmitis can be defined as an inflammation of intraocular tissues associated with hypopyon, and loss of retinal red reflex.¹ This intraocular infection is established due to seeding of organisms during intraocular surgery as a post-operative endophthalmitis, after penetrating injury as post-traumatic endophthalmitis, due to infection elsewhere in the body as endogenous endophthalmitis. Endophthalmitis is the infection which occurs in a closed space. Replication of bacteria can result in to rapid destruction of underlying tissue. Untreated or misdiagnosed cases result into deterioration in visual acuity leading to blindness.²

In different local (national) studies, the incidence of post operative infective endophthalmitis has

been reported as 4.5% in 2005,³ and 4% in 2008.⁴ The global incidence of post operative endophthalmitis has decreased remarkably in last ten years i.e., from 0.7% to 0.3%.^{5,6} In a study conducted in 2010 the rate of acute post-operative endophthalmitis in cataract surgery has declined to 0.028%.⁷

The susceptible gram positive organisms in bacterial endophthalmitis are *Staphylococcus aureus*, streptococci, and enterococcal species. Gram negative isolates include *pseudomonas*, *haemophilus influenzae* and *enterobacter*.⁸

Intravitreal injection of antibiotics on the first day of diagnosis is the treatment of choice for post-operative infective endophthalmitis. The blood retina barrier does not allow systemically administered antibiotics to pass into the vitreous cavity.⁹ On the other hand the antibiotic injected through intravitreal route cross the barrier uninterrupted and directly pass in to the intraocular cavities. A single injection with therapeutically effective and non toxic dosage is quite enough to cure intraocular infection.⁹ Sometimes a repeat dose is required for virulent organisms. The intra vitreal antibiotics presently available to work against Gram-positive organisms are: Vancomycin & Cefazoline.⁹

The drug of choice to combat infection by Gram-negative organisms is ceftazidime (cephalosporin). It is a third generation broad-spectrum antibiotic.¹⁰ Ceftazidime inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins thus inhibiting peptidoglycan synthesis in bacterial cell walls, and cell wall biosynthesis. As a result the bacteria eventually are killed due to activity of cell wall autolytic enzymes.⁹ Ceftazidime is now being frequently administered alone and combined with vancomycin without producing any retinal toxicity. The objective of this study was to obtain promising results regarding media clarity and improved visual acuity in response to intravitreal ceftazidime used in the management of acute post-operative endophthalmitis.

METHODOLOGY

This is a seventy eight months retrospective clinical analysis of patients who had suffered from acute-onset postoperative endophthalmitis reporting at a tertiary eye care centre. The subjects of both sexes operated at different primary and secondary eye care centers of the region presenting for the first time between March 2004 and August 2010 were incorporated in this study.

Inclusion Criteria: Patients of different age group having been operated for cataract and intraocular

lens implantation, glaucoma filtration procedures and other types of intraocular surgery associated with acute bacterial endophthalmitis within first fifteen days post operative and with best corrected visual acuity of hand movements and better were included.

Exclusion Criteria: The subjects having endophthalmitis more than fifteen days post operative, fungal endophthalmitis, history of post operative trauma and repeat intraocular surgery, visual acuity of perception of light and worse and associated retinal detachment were excluded from this work. All the registered patients were examined in the out patient department. After going through the informed consent discussion successfully, the subjects were assessed for age, gender, residency and occupation, history of intraocular surgery and duration of onset of clinical features of post-operative endophthalmitis.

Physical examination included best corrected visual acuity for normal and affected eye, using Snellen's chart and E-chart for illiterates. Anterior segment Slit lamp examination was performed for confirmation of signs of endophthalmitis. Direct ophthalmoscopy at one meter and Posterior segment slit lamp examination with 90D bi-spheric condensing lens was done for the presence or absence of retinal red reflex through pupil, and vitreous exudates.

Intraocular pressure was measured by applanation tonometer. B-Scan ultrasonography was performed in co-operative patients. All subjects with clinical evidence of endophthalmitis were admitted. After obtaining written permission, intravitreal injection ceftazidime was administered on the day of diagnosis with the following preparation; 2.2 cc of saline was injected to 500 mg vial of ceftazidime.

Table-I: Demographic Information: n= 39

Sex	N/O Pts	Percentage (%)
Male	28	71.7
Female	11	28.3
Age (Years)		
Up to 20	09	23.1
21 to 40	13	33.3
41 to 60	17	43.6
Residency		
Rural	23	59.0
Urban	16	41.0
Financial Status		
Upper	02	05.1
Middle	12	30.7
Lower	25	64.2



Fig.1: A 55 year male admitted at Liaquat University eye hospital suffering from right eye acute post-operative endophthalmitis.

After gently mixing the solution, 0.1 cc was drawn in a syringe already containing 0.9 cc of saline solution to make 1cc (22.5 mg/cc of ceftazidime). 0.9 cc of saline from the syringe was discarded to save 0.1 cc (concentration of 2.25 mg) /cc of ceftazidime solutions ready for intravitreal injection.

Topical anesthesia was induced with Xylocaine 4% ophthalmic drops instilled on cornea. 5% povidone iodine solution was used on the globe, lids and surrounding skin to achieve disinfection. After five minutes the ocular surface was gently washed with balanced salt solution. The wire eye lid speculum was placed and a sub-tenon injection of xylocaine 2% was given at the distance of 3.5mm from Corneo scleral junction on outer inferio temporal side. A 25 gauge needle on 3 cc disposable syringe was injected in to the anterior vitreous cavity 3.5 mm behind limbus to aspirate 0.2ml of vitreous if possible. Keeping the needle in place the syringe was replaced with another syringe containing injection ceftazidime 2.25mg in 0.1ml. The drug was injected with continuous push postero medially away from macula. The needle was slowly with drawn. The patient was advised to sit with face down position for five minutes to avoid drug settling on macula. The vitreous aspirate was labeled and sent along with patient's Performa for identification of isolates.



Fig.2: 48 hours after 1st intra vitreal injection ceftazidime, the fibrin exudate in the pupillary area is shrinking.

Cycloplegia was induced using topical atropine 1% or homatropine 2% ophthalmic drops. Topical half hourly antibiotic drops consisting of 50% ceftazidime were also used round the clock for first 36 hours. The subjects responding well were also given systemic steroids. Intra vitreal ceftazidime was repeated in poorly responding patients after 48 hours of first injection. Vitrectomy was strongly advised to the subjects showing worsening of condition after two consecutive intra vitreal injections. The criteria for better recovery was reduction in pain, improvement of vision, resolution of hypopyon, shrinking of fibrin exudates, clearing of anterior chamber, and recovery of retinal red reflex through pupil. The follow up was done on second week, 8th week, and end of third month. The final visual acuity was documented on twelfth week post treatment outpatient visit. All the subjects were requested to complete post treatment follow up.

RESULTS

Out of thirty nine registered patients having been diagnosed as post operative endophthalmitis, thirty four (87.1%) were given intra vitreal ceftazidime on first day (Fig.1). Five subjects did not accept the treatment and were discharged on request. Patient's data regarding sex, age residency etc is mentioned in Table-I.

The vitreous tap of twenty three (67.6%) patients was performed successfully. According to culture

Table-II: Visual acuity before and after Intra Vitreal Injection Ceftazidime: n = 34

N/O Pts	V/A on 1st Visit	N/O Injections	V/A after 2nd W	Int. Vit. 8th W	Injection 12th W	Percentage %
11	HM+	One	6/24+	-	-	32.4
14	HM	One	CF	6/60+	6/36+	41.2
04	HM	Repeat	CF	6/60	6/60+	11.7
05	HM	Repeat	HM	-	-	14.7

V/A=Visual acuity; Int=Intra; Vit=Vitreal; W=Week; HM=Hand Movements; CF=Counting Finger; + = Better.

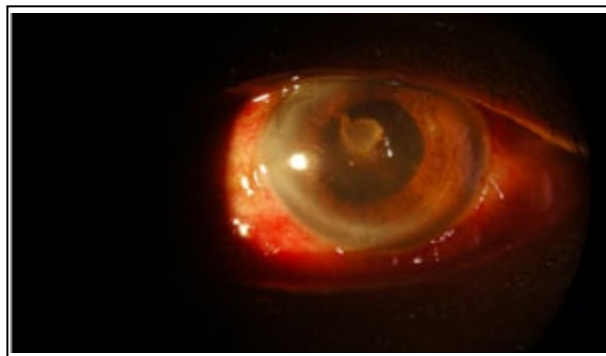


Fig.3: 96 hours after intra vitreal ceftazidime injection, pupil is dilated, inflammation is almost resolved with small calcified membrane in central pupillary area.

sensitivity results, *Staphylococcus Aureus* was isolated in eleven (47.8%) subjects. *Staphylococcus Epidermidis* was detected in five (21.7%) and *streptococcus pneumoni* in one (4.3%) patient. The vitreous culture sensitivity results of six patients (26.2%) could not be obtained.

Out of thirty four patients, eleven subjects who improved quite well in second week after intra vitreal injection were lost to follow up. Nine subjects were given repeat intra vitreal ceftazidime and five were referred to vitreo retina department. Remaining eighteen completed the post treatment follow up criteria of this study. The visual acuity recorded at first visit and after intravitreal injection ceftazidime 2.25mg is summarized in Table-II (Fig 2 - 4).

DISCUSSION

The aim of antimicrobial treatment for endophthalmitis is to provide rapid sterilization of vitreous cavity. The preferred therapeutic agent should be able to achieve appropriate intravitreal concentration suitable to eradicate isolates, avoid iatrogenic ocular tissue damage and preserve normal integrity of intraocular structures.

Post-operative endophthalmitis is one of the serious complications leading to loss of vision. Gram-positive and Gram-negative organisms both are supposed to be the main culprits causing acute postoperative endophthalmitis.⁸ Intravenous antibiotics have no effect on such a devastating condition.¹¹

The intravitreal injection of appropriate antibiotics within recommended dose achieves immediate therapeutic vitreous concentrations and provides better effect against many organisms encountered in the postoperative settings of infection. It also helps avoid potential systemic side effects.



Fig.4: Right eye after 3 weeks of intra vitreal ceftazidime. (V/A = 6/12).

Ceftazidime being a semi-synthetic, broad spectrum antibiotic exhibits a bactericidal activity. It offers an expanded gram-positive and gram-negative coverage when injected intra- vitreally and inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins. As a result the bacteria are completely destroyed.^{12,13}

After intra vitreal injection, ceftazidime leaves the vitreous cavity through retina.¹¹ Due to its non-toxic nature the ceftazidime can also be safely repeated in poorly responding conditions. In our study intravitreal ceftazidime injection was repeated in nine (26.4%) subjects. In one national study,¹⁴ it was repeated in 24.0% cases. Most specifically 100% Gram-negative ocular isolates are sensitive to ceftazidime, a third-generation cephalosporin.¹⁵

However, in the current study we have shown that ceftazidime produces promising results after intravitreal injection i.e., 85.3% subjects with V/A 6/60 and better. These statistics can be compared with one study¹⁶ which showed the post treatment V/A of 6/60 and better in 84% subjects. In another study by Kumar et al,¹⁷ the success rate was 92.4% which is slightly higher than our study. In our study we had better ratio of vitreous culture positive cases.

Although an intravitreal injection is a relatively safe procedure, it is not completely without risk. The risks include retinal trauma, vitreous haemorrhage, and retinal detachment¹⁷ In our study, neither of these complications was encountered. The over dosage of drug in the vitreous cavity is harmful and can lead to retinal toxicity. Therefore, the surgeon has to be extremely cautious about injecting correct dose of antibiotics, preparing the injection carefully and observing the patient closely in post treatment follow up visits.

CONCLUSION

Acute post-operative endophthalmitis has always remained a major clinically devastating problem for the ophthalmic surgeon. Ceftazidime is an appropriate and rational option in such complicated situations.

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