Original Article

Effectiveness and Safety of Intracameral Ceftazidime Injection in Phacoemulsification

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Abstract

Background: *Cataract is the number one cause of blindness worldwide, which is curable with simple removal of cataractous lens and IOL implantation. But cataract surgery is complicated by postoperative infection (endophthalmitis) mainly that can lead to loss of sight or even loss of the eye. But it has been observed in some cases; with a very good and uneventful cataract surgery patient's vision may not improve without any preexisting ocular disease. Patient as well as surgeons become tense in this aspect. In this case this is not due to infection, but some other factors are responsible for poor vision. It is speculated that intraocular tissue reaction towards the fluidics, intracameral antibiotic, efficiency of surgeon and the machine used may have contributed to this. We have tried to evaluate the ocular tissue effect with intracameral ceftazidime along with ringer's lactate solution. However, it is also used as a prophylaxis of endophthalmitis. It is now time to demand study to evaluate safety aspects of the intracameral ceftazidime used in phacoemulsification. The objective of the study is to evaluate the safety profiles of intracameral ceftazidime in phacoemulsification.* ***Materials and Methods:*** *The prospective interventional study was conducted at National Institute of Ophthalmology & Hospital, Dhaka, Bangladesh from January 2022 to June 2022 with ethical clearance from respective IERB. Sixty patients were selected and half (30) of them receive intracameral ceftazidime (1 mg in 0.1 ml) and the rest (30) of them receives ringer's solution 0.1 ml - given intracamerally at the end of phacoemulsification. Central endothelial cell density (ECD), central corneal thickness (CCT) and central retinal thickness (CRT) were determined by specular microscopy, pachymetry and ocular coherence tomography, respectively, preoperatively, at 7th postoperative day and 3 months after surgery.* ***Results:*** *This study showed no statistically significant differences in the changes of ECD, CCT and CRT between eyes receiving intracameral ceftazidime and control.* ***Conclusion:*** *The use of intracameral ceftazidime (1 mg in 0.1 ml solution) at the time of phacoemulsification had no significant effect on ECD, CCT and CRT postoperatively.*

Keywords: Cataract, Phacoemulsification, Intracameral Ceftazidime.
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Introduction

Cataract is the most common cause of reversible blindness in the world and the most common forms of it are not still prone to effective prevention and great efforts are therefore being made to provide sight-restoring surgery[1]. Bangladesh is part of the Southeast Asia region of the World Health Organization, which comprises a quarter of the world's population, but is estimated to comprise a third of the world's 45 million blind. Cataract is responsible for approximately 80% blindness in this region. Rapid population growth, especially among the elderly, coupled with low cataract surgical output (in certain countries) has resulted in an ever-growing cataract backlog[2]. The only known treatment for cataract is surgical removal and subsequent correction of the optical error that develops[3]. Improvements in surgical technique over the last decade, particularly the routine use of phacoemulsification allowing small suture less incisions and continuous curvilinear capsulorhexis ensuring in-the-bag placement of the intraocular lens (IOL), have improved the predictability of postoperative refraction[4]. But cataract surgery is complicated by postoperative infection (endophthalmitis) mainly that can lead to loss of sight or even loss of the eye. But it has been observed in some cases, with a very good and uneventful cataract surgery patient's vision may not improve without any preexisting ocular disease.

Patients as well as surgeons become tense in this aspect. In this case this is not due to infection, or to

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some other factors for poor vision. It is speculated that intraocular tissue reaction towards the fluidics, intracameral antibiotic, efficiency of surgeon and the machine used may have contributed to this. We have tried to evaluate the ocular tissue effect with intracameral ceftazidime along with the ringer's lactate solution. However, it is also used as a prophylaxis of endophthalmitis. Intracameral drug toxicity may cause endothelial cell death or spread to the posterior segment of the eye, where it may cause macular edema. The European clinical trials did not report on ceftazidime's effects on macular thickening or endothelial cell loss. In this prospective randomized clinical trial, we directly compared the safety profiles of ceftazidime.

The corneal endothelium consists of a monolayer of cells on the posterior corneal surface that has limited regeneration capability after injury. The barrier function and the active fluid pump of corneal endothelial cells preserve the cornea's normal thickness and transparency[5]. The natural loss of human endothelial cells is approximately 0.6% each year[6]. Intraocular procedures, like phacoemulsification cataract surgery, generate turbulence from fluid and lens fragments, which can result in damage to the endothelial cells[7]. Using fortified balanced salt solution (BSS) as irrigating solution, the mean cell loss at 2 months was 13.2% (±2%) in Lucena et al. study[8] and 22.9% (±14%) at 3 months in the Richard et al. study[9]. Various in vivo investigations employing different irrigating solutions demonstrate that postoperative corneal thickness and endothelial cell count depend on the chemical makeup of the solution rather than irrigation volume and duration[10-13]. Nevertheless, it has been demonstrated that rinsing with dextrose bicarbonate Lactated Ringer's solution during cataract surgery works almost as well as enriching BSS[14]. Cefazolin is a first-generation cephalosporin that has bactericidal effect against Gram-positive cocci, particularly staphylococci. Ceftazidime, a third-generation cephalosporin, was used in Sweden following an epidemic caused by a Gram-negative bacterium[15].

Materials and Methods

This study was approved by the Ethical Review Committee of National Institute of Ophthalmology & Hospital (NIO&H), Dhaka. Patients aged 50-60 years with grade-II senile cataract were selected through the inclusion and exclusion criteria from the cataract unit of this hospital. Only one eye in a patient with bilateral cataract was selected in this study. After selection of patients, a comprehensive ocular examination was performed. Written informed consent to the study was obtained from those who satisfied inclusion criteria. After this, keratometry, biometry, pachymetry, central endothelial cell density (ECD) and central retinal thickness (CRT) were measured in a standard setting. Macular thickness was determined using time-domain optical coherence tomography (OCT). After proper evaluation patients were admitted to cataract unit, National Institute of Ophthalmology & Hospital, Dhaka. Preoperative topical broad-spectrum antibiotic (moxifloxacin 0.3%) 1 drop 8 hourly was started one day before operation. Pupils were dilated with tropicamide 0.8% + phenylephrine 5% eye drop by 1 drop 5 minutes interval for 3 times, half an hour before operation. Patients were randomized to the operating list of participating single surgeon. In every patient local anaesthesia was given as peribulbar anaesthesia just before operation.

All the phacoemulsification surgery was done by single surgeon. A single plane clear corneal incision at temporal side was made. Ringer's solution was used in phacoemulsification as cheap, available and as effective as BSS. Foldable IOL was implanted in bag (capsular bag). The corneal wounds were hydrated with the ringer's solution. Injection ceftazidime 1% (1 mg in 0.1 mL) was given in to the anterior chamber (AC) of eye after completion of phacoemulsification in 30 patients. That was prepared from injection ceftazidime (250 mg/vial) with normal saline and dispensed into a 1-mL tuberculin syringe with 26 G AC cannula. We use normal saline to dissolve the injection ceftazidime to avoid hypotonicity of solutions as Lam, et al.[16] use in their study. The injection ceftazidime solution was prepared from the powder supplied in vial (250 mg) for intravenous use. The powder was first dissolved with 5 mL normal saline (NS = 0.9% NaCl) to a concentration of 50 mg / mL with a 5-mL syringe. Then 1 mL (50 mg) dissolved solution was taken into 5-mL syringe and diluted up to 5 mL to the concentration of 10 mg/mL with NS. Then 1 mL solution was taken into 1-mL insulin syringe. The procedure did not involve the use of BSS or water for injection. A hypotonic solution could result from dissolution and dilution with water for injections. Ceftazidime combined with BSS has the capability to form precipitations. Four hours after reconstitution, the solutions were discarded. The rest of the 30 patients receive no intracameral (into AC) antibiotic injection after phacoemulsification. Subconjunctival steroid injection (Dexamethasone 0.5 mL) was given in inferior fornix. The eye lids were closed and dried then the pad bandage was given. The surgeon was masked as to which treatment was given until the surgery had been completed and the patient had left the operation theater. A standard topical antibiotic + steroid regime (moxifloxacin 0.3% solution and prednisolone acetate 1% suspension) was started on the first postoperative day. Patients were seen again at 1 week, 1 month, and 3 months (±2 weeks) after operation. Central ECD and CRT were measured at

7th post operative day (POD) & 3 months (±2 weeks) postoperatively and pachymetry (CCT - central corneal thickness) at 1st week and 3 months (±2 weeks) by the same trained senior staff nurses masked to the treatment, previous specular microscopy and OCT data. The primary outcome variables were changes in ECD, CCT and CRT. Change in ECD was expressed as a percentage, obtained by dividing the difference between postoperative and preoperative values by the preoperative value. Change in CCT was expressed as a percentage, obtained by dividing the difference between postoperative and preoperative values by the preoperative value. Similarly, the percentage change in CRT was obtained by dividing the difference between post and preoperative thickness by the preoperative value.

Results

A total of 60 patients (30 cases & 30 controls), comprising 40 males and 20 females, were selected in this study. The patients' average age was 54.3 years. They were randomized to be operated by single surgeon. The two groups were comparable regarding their mean age, visual acuities, baseline ECD, CCT and CRT. The mean preoperative unaided visual acuity (VA) was 6/36 recorded by Snellen chart method. The range of improvement of VA after cataract surgery was 6/9 to 6/6. Maximum (90%) patients regain their vision 6/6 at last follow up (3 months ± 2 weeks). The mean pre- and postoperative ECD in case were 2,754 and 2,517 cells/mm^2, respectively. The mean pre- and postoperative ECD in control were 2,717 and 2,470 cells/mm^2, respectively. The endothelial cell count was done with a specular microscope before the day of operation, at 7th POD and 3 months postoperatively. The mean change was −8.6% and −9.0% in case and control respectively (Table-I).

The mean pre- and postoperative CCTs in case were 545 and 559 µm. The mean pre- and postoperative CCTs in control were 547 and 560 µm. The central corneal thickness was measured with a pachymeter before the day of operation at 7th POD and 3 months postoperatively. The central corneal thickness was increased in the 1st follow up but normalized at last follow up (3 months ± 2 weeks). The mean change was 2.5% and 2.3% in case and control respectively (Table-II). The mean pre- and postoperative CRTs in case were 177 and 183 µm. The mean pre- and postoperative CRTs in control were 176 and 182 µm. The central retinal thickness was measured with optical coherence tomography before the day of operation, at 7th POD and 3 months postoperatively. The mean change was 3.3% and 3.4% in case and control respectively (Table-III). We were unable to detect a statistically significant change in ECD, CCT and CRT between ceftazidime and control (p>0.05). Table- I shows the changes in postoperative endothelial cell density between cases and controls which were 8.6% and 9.0% with the p-value >0.05. Table-II shows the changes in postoperative central corneal thickness between cases & controls which were 2.5% and 2.3% with the p-value >0.05. Table-III shows the change in postoperative central retinal thickness between cases & controls which were 3.3% and 3.4% with the p-value >0.05.

Table-I: Postoperative change in endothelial cell density (ECD) in cases and controls (n=60)

ECD (cells /mm^2)	Cases (n=30) (cells/mm^2)	Controls (n=30) (cells/mm^2)	p-value
Pre-operative	2,754	2,717	>0.05
Post-operative	2,517	2,470	
Change (%)	-8.6	-9.0	

Table-II: Postoperative change in central corneal thickness (CCT) in cases and controls (n=60)

CCT (µm)	Cases (n=30) (µm)	Controls (n=30) (µm)	p-value
Preoperative	2,754	2,717	>0.05
Postoperative	2,517	2,470	
Change (%)	-8.6	-9.0	

Table-III: Postoperative change in central retinal (macular) thickness (CRT) in cases & controls (n=60)

CRT (µm)	Cases (n=30) (µm)	Controls (n=30) (µm)	p-value
Preoperative	177	176	>0.05
Postoperative	183	182	
Change (%)	3.3	3.4	

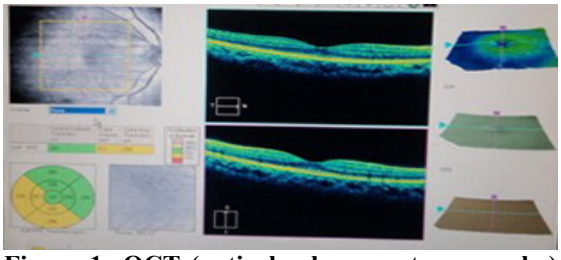

Figure-1: OCT (optical coherence tomography) picture showing retinal thickness.

Discussion

Phacoemulsification is probably most widely used for cataract surgery now a days[4]. In this study we used intracameral ceftazidime 1 mg in 0.1 mL at the end of phacoemulsification in 30 cases and compared the safety of the drug with control group. In control group intracameral ceftazidime was not

used at the end of phacoemulsification. BSS was applied as the control in a study by Gupta, et al.[16] on the safety of intracameral cefuroxime. We used ringer's solution as control to differentiate the effect between ceftazidime and ringer's solution, if such existed, and to avoid the confounding effect of a control that was different from the diluent. The risk of drug toxicity causing toxic anterior segment syndrome can occur from errors in dilution and dosing. We discarded ceftazidime solution 4 hours after reconstitution to avoid possible loss of efficacy, despite the manufacturers confirmed compatibility with NS and retaining potency more than 12 hours after reconstitution[5]. In this study design, control for sources of variations was addressed. Patients with long axial lengths (thin maculae) and any systemic or ocular diseases that may cause postoperative macular edema were not included in our sample. In this study we use single surgeon for phacoemulsification to avoid surgeon's factors for outcome variables. Single surgeon performing the procedure could limit variations from surgeons in clinical trials comparing the effects of irrigating solutions or phacoemulsification methods on the cornea[6,7].

In our study the mean corneal endothelial cell loss was 8.6% in case and 9.0% in control that was closely related with others study. Lam, et al.[17] shows the mean endothelial cell loss was 9.9% in their study done by four surgeons compared favorably with the results in two recent studies on endothelial cell loss in phacoemulsification. In Lucena, et al.[8] study the mean cell loss at two months was 13.2% (±2%) with fortified BSS as the irrigating solution and 22.9% (±14%) at 3 months in the Richard, et al.[9] study. The mean cell loss in eyes operated on by one participating surgeon was 19.8%. This value was comparable to the mean cell loss by Richard, et al.[9] study. In this study, 50 or more endothelial cells per frame were accepted for analysis. There was an inherent variability in the measurement of ECD. Variations could be reduced by cell analysis over a larger area or with repeated measurements.

In practice, the area of endothelial cells available for counting was controlled by magnification and the area brought under focus of the specular microscope. We did not compare the absolute cell loss as Montan, et al.[18] did in their study on the safety of intracameral cefuroxime. Anticipating a wide range of preoperative cell densities (ranging from 2,470 to 3,057 cells/mm^2), we analyzed the percentage changes rather than the absolute differences between the pre- and postoperative ECD values. The percentage values could be used to illustrate how many cells were lost in relation to the baseline ECD. We measured ECD before operation, at 7th POD and 3 months (±2 weeks) postoperatively. In a study by Lucena, et al.[8] comparing the changes in the cornea following phacoemulsification with lactated Ringer's solution versus fortified BSS, the endothelial cell counts stabilized 2 weeks after surgery. The medication was less likely to result in ongoing endothelial cell loss, and the effect might be observed if the measurements were made later.

In this study the mean increase of central corneal thickness (CCT) was 14.0 µm in the case and 13.0 µm in the control group in postoperative period, normalized at last follow up (3 months ± 2 weeks) that was closely related with another study[9]. The researchers studied central corneal thickness in phacoemulsification with BSS Plus Ringers Lactate solution. There was a significant increase in CCT in both groups between 8 and 30 days after surgery. In both groups, the mean CCT returned to baseline levels 60 days following surgery. This study results showed a mean increase of central retinal thickness (CRT) 3.3% (6.0 µm) in case and 3.4% (6.0 µm) in control group in the postoperative period. In a study by Kurz, et al.[19] demonstrated a 6-8 µm increase in CRT at 8 weeks after micro-incisional cataract surgery. Kim, et al.[20] showed a mean 9 µm increase in CRT in 12 weeks. Biró, et al.[21] advocated using the 6 mm perifoveal retinal thickness for a more sensitive measure for detecting macular edema and showed 5.3% increase in 6 mm perifoveal values at two months after phacoemulsification. The increase was maximal at 1 month postoperatively. To study the effect on macular thickness, we used CRT as our primary outcome variable like the study by Kim, et al.[20] No topical nonsteroid anti-inflammatory agent (NSAID) was used in the pre and immediate postoperative stage. This could have masked the difference in change of macular thickness, if any, between the groups. We were unable to detect any statistical difference in CRT between treatment and control groups.

Limitation

The study was done with small samples and short duration.

Conclusion

The use of intracameral ceftazidime 1 mg in 0.1 mL in of phacoemulsification is safe regarding the change in corneal endothelial cell density (ECD), central corneal thickness (CCT) and central retinal thickness (CRT).

Conflict of Interest

The authors declared that they have no conflicts of interest.

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