

Comparison of Post-operative Endophthalmitis prophylaxis using Intracameral cefuroxime and moxifloxacin in rural Pakistan- A randomized controlled trial

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ABSTRACT

Objective: To compare the efficacy and safety of Intracameral Cefuroxime and Moxifloxacin in preventing postop endophthalmitis in rural areas.

Study Design: A Randomized controlled trial

Place and Duration: At Layton Rehmatullah Benevolent Trust (LRBT) Free Secondary Eye Hospital, Akora Khattak, from 1st January 2010 till 31st January 2011.

Methodology: Patients undergoing cataract surgery were randomly distributed in three groups A, B and C. Group A underwent routine aseptic technique of phacoemulsification without Intracameral antibiotic injection of any kind. Group B after routine phacoemulsification received an additional Intracameral Cefuroxime injection in the dose of 1mg/0.1ml at the end of surgery while Group C after routine phacoemulsification received Intracameral Moxifloxacin 5%. Patients were followed for four weeks post operatively and frequency of Endophthalmitis was noted in the patients. Post-operative visual acuity and reaction in the anterior chamber was also noted.

Results: A total of 908 patients were operated for cataract surgery during this period. The mean age of patients in all the groups was 60 years and 56% of the patients were males. The frequency of post op endophthalmitis was 1.2% in Group A, whereas the frequency was 0% in both Group B and C. There was trace to +1 cells in the anterior chamber on the first post op day in 84% of patients in the group A, 97% of patients in group B and 95% of patients in group C. However, there was no reaction one week post op in 95% of patients in group A, 98.8% of patients in group B and 97.8% of patients in group C. Initial results reflected that there were fewer cases ($P < 0.05$) of post op endophthalmitis following Intracameral antibiotic injections.

Conclusion: Intracameral use of cefuroxime and moxifloxacin is effective in controlling post-operative endophthalmitis in rural Pakistan with high frequency of cataract surgeries without untoward side effects.

Keywords: Post-operative, Cataract, Endophthalmitis, Intra cameral, Cefuroxime, Moxifloxacin

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INTRODUCTION

Infective endophthalmitis is a devastating postoperative complication of cataract surgery. This potentially blinding complication is every cataract surgeon's nightmare. The incidence of endophthalmitis after cataract surgery is stated to be 0.1% to 0.24%^{1,2}. Most of the endophthalmitis occurs from contamination of bacteria from patients own flora. The most common bacteria involved in post op endophthalmitis is coagulase negative staphylococcus, Streptococcus Viridans and Staphylococcus aureus²⁻⁵. Once the infection is there it is very difficult to control and most of the eyes end up losing useful vision if not treated promptly. It is for this reason the role of prevention is very important.

Over the years different pre and postoperative measures for its prevention have been advocated. Use of antiseptic agents like povidone- iodine in the conjunctival sac is effective in ocular surface decontamination and has significantly proven efficacy^{4,6,7}. Research has also found that modern fluoroquinolones reduce infection in the ocular flora⁸. However, the most

landmark of all the studies is the ESCRS study on endophthalmitis prophylaxis¹. This European Society of Cataract and Refractive Surgeons study revealed that use of Intracameral cefuroxime decreases the rate of post-operative endophthalmitis to five folds. The study also validated the Intracameral route of antibiotic delivery as effective for endophthalmitis prophylaxis. Additional studies^{9,10} have also determined Intracameral levofloxacin and moxifloxacin to be effective in controlling post op endophthalmitis without any untoward side effects.

In this study we have tried to find an easy and effective way to prevent post-operative endophthalmitis in rural Pakistan. We have selected the Intracameral route of delivering antibiotics to the eye prophylactically because it is the most direct way of introducing antibiotic to the site of infection. Also it can be done by the surgeon at the time of surgery and doesn't have to rely on the patient for its delivery. Also when bulk surgeries are being performed these antibiotics become more cost effective. So this study was conducted with an objective to compare the efficacy and safety of Intracameral Cefuroxime and Moxifloxacin in preventing postop endophthalmitis in rural areas.

METHODOLOGY

This randomized controlled trial was conducted at LRBT Free Secondary Eye Hospital, Akora Khattak in Khyber Pakhtunkhwa province of Pakistan from 1st January 2010 to 31st January 2011, after ethical approval from the LRBT Ethics Review Committee. All adult patients undergoing phacoemulsification during this period were included in the study. Patients with glaucoma, corneal opacities, diabetic retinopathy, maculopathy of any other pathology, active uveitis and a complicated phacoemulsification were excluded from the study.

Patients were randomly allocated in three groups. Group A received no Intracameral antibiotic at the end of routine phaco. Group B received an Intracameral injection of Cefuroxime (1mg in 0.1ml) at the end of surgery and Group C received an Intracameral injection of Moxifloxacin (0.1ml of 5%) at the end of surgery.

On the day of surgery all the patients were given two tablets of 250mg acetazolamide and a single tablet of 500mg ciprofloxacin. Topical ciprofloxacin and ibuprofen were also instilled before the surgery. A routine phacoemulsification using the stop and chop technique was performed after complete asepsis by a single surgeon through a 3 mm sclero-corneal incision. At the end of surgery the incision was enlarged to 5.6mm to implant a PMMA no foldable IOL in the bag. Corneal wound was hydrated and sealed. At the end of surgery a sub conjunctival injection of Gentamycin and triamcinolone was given. Patients in group B and C received additional intracameral cefuroxime and moxifloxacin respectively.

Post operatively all patients received 500mg ciprofloxacin BD for three days. Topically they were given eye drops of combined chloramphenicol and dexamethasone hourly for the first 24 hours. The drops were reduced to four times a day

after that for four weeks. Patients were followed on day 1, day 7 and day 30 after the surgery.

Endophthalmitis was diagnosed clinically when a patient presented in the first week after surgery with pain, reduced vision, severe AC reaction with hypopyon and no fundus view on dilated funduscopy. Besides endophthalmitis the best corrected visual acuity and anterior chamber reaction was also noted to assess the safety of Intracameral medicines.

Data Analysis: The data was recorded and retrieved through hospital information management system and the results were compared by independent samples T test using SPSS version 20.

RESULTS

A total of 908 eyes of 908 patients were included in the analysis. Out of these 247 eyes (27%) were in group A, 337 eyes (37%) were in group B and 324 eyes (36%) were in group C. The mean age of patients in all the three groups was 60 years (SD± 4.9) approximately with 90% of the patients within the age group of 55-65. Approximately 56 % of patients were males and 44% of patients were females.

In group A there were 3 (1.2%) cases of clinical endophthalmitis whereas there were no such cases in group B and group C and (P value <0.05) (Table-I).

Table-I: Summary of Frequency of different variables (N=908)

Variables	Group A (Control Group) (n=247)	Group B (Inj Cefuroxime Group) (n=337)	Group C (Inj Moxifloxacin Group) (n=324)
Frequency of post op Endophthalmitis	3 (1.2%)	0 (p 0.045)	0 (p 0.047)
Post op Visual Acuity (≥6/9)	216 (87%)	333 (98%)	303 (93%)
Post op AC reaction (Trace to +1Cells) First post op day	207 (84%)	328 (97%)	309 (95%)
Post op AC reaction (None) one week post op	236 (95%)	333 (98.8%)	317 (97.8%)

Besides the control of endophthalmitis, patient's Visual acuity and anterior chamber reaction were also analysed. In group A the post op visual acuity was better than 6/9 in 87% (N-216) of eyes where as in group B and C the post op visual acuity better than 6/9 was found in 98% (N-333) and 93% (N-303) of the eyes (Table II).

Table-II: Post-operative Visual Acuity (N=908)

Groups	Total No of Patients in each Group	Post-Operative Visual Acuity			
		Visual Acuity ≥ 6/9		Visual Acuity < 6/9	
		No of Patients (n)	Percentage (%)	No of Patients (n)	Percentage (%)
A	247	216	87%	31	13%
B	337	333	98%	4	2%
C	324	303	93%	21	7%

The study also shows that the trace to +1 cells were seen in the anterior chamber on the first post op day in 84% (N-207) of eyes in group A, 97% (N-328) of patients in group B and 95% (N-309) of patients in group C (Table-III). However there was no reaction one week post op in 95% (N-236) of patients in group A, 98.8% (N-333) of patients in group B and 97.8% (N-317) of patients in group C. (Table-IV)

Table-III: Anterior Chamber Reaction on First post op day (N=908)

Groups	Anterior Chamber Reaction on First post op day						Total
	none	trace to +1	+2	+3	+4/m3m branes	hypopyon	
A	25 (10%)	207 (83%)	12 (5%)	2 (1%)	0	1 (1%)	247
B	1 (0.5%)	328 (97%)	6 (1.5%)	1 (0.5%)	1 (0.5%)	0	337
C	7 (2%)	309 (95.5%)	8 (2.5%)	0	0	0	324
Total	33	844	26	3	1	1	908

Table-IV- Anterior Chamber Reaction after One week (N=908)

Groups	Reaction in Anterior Chamber One week Post op				Total
	none	trace to +1	+4/membrane	hypopyon	
A	236(95.5%)	8(3%)	1(0.5%)	2(1%)	247
B	333(99%)	4(1%)	0	0	337
C	317(98%)	7(2%)	0	0	324
Total	886	19	1	2	908

DISCUSSION

Post-operative endophthalmitis is the most devastating and dreaded complication after cataract surgery. In our study the frequency of endophthalmitis was 1.2% in group A (control group). This is almost similar to what is mentioned in a study conducted in North West Frontier province (now KPK) of Pakistan by Wade et al, where the incidence of endophthalmitis was 1.6%¹¹. This is in contrast to another study conducted by Narsani et al in Hyderabad, Sind¹² where the incidence was 0.65% which is much lower than our study. The incidence in Narsani's study is much closer to international literature. Multiple international studies^{1,2,13} have reported the incidence of post op endophthalmitis to be around 0.1 to 0.24%. A study by Caravaca et al¹³ mentions the cumulative incidence to be around 0.23% which is almost similar to the incidence mentioned by ESCRS study (0.24%)¹. Since the findings of these studies the prophylactic use of Intracameral antibiotics has become more common and the incidence has gone further down. The Meta analysis conducted by Linertova et al confirms that the incidence of this dreaded complication has gone down to 0.01-0.06% since the use of Intracameral Cefuroxime injection¹⁴. The study we conducted show a much higher incidence. This could be because the setting of this study was a field hospital in rural Pakistan, where the poverty and illiteracy level was high thereby resulting in poor hygienic standards and subsequent noncompliance to post op

instructions. Another contributory factor could be that high volume surgeries in such field hospitals leads to compromised sterilization procedures hence resulting in post op infections. In this study there were no cases of endophthalmitis in the groups in which we used Intracameral cefuroxime (group B) and Intracameral moxifloxacin (group C). The literature also indicates that the rate of endophthalmitis is considerably reduced by the use of Intracameral antibiotics. The land mark clinical trial of ESCRS by Barry et al recorded a six fold decrease in the post op endophthalmitis rate after the use of Intracameral cefuroxime¹. Since then a number of studies have shown a considerable decline in the rate of post op endophthalmitis¹⁴. A recent study conducted by Haripriya in southern India show a seven fold reduction in rate of post op endophthalmitis since the use of post op Intracameral moxifloxacin¹⁵. A Cochrane review by Gower E W also established the reduction in the rate of post op endophthalmitis after using Intracameral antibiotics¹⁶. Similar results were seen in our study with 0% incidence of post op endophthalmitis after the use of Intracameral antibiotics which was statistically significant ($p < 0.05$).

The safety of Intracameral antibiotics was also evaluated in our study. The post op AC reaction was mild on day one and resolved within one week in 97% of patients in the groups B and C. The post op visual acuity was also better than 6/9 in 98% and 93% of patients in Group B and C. The safety of Intracameral antibiotics have been established by multiple studies. A large French study by Daïen et al looked for difference in the risk for cystoid macular edema between the group that received and did not receive Intracameral cefuroxime; there was no increased risk in either group¹⁷. Another study conducted by Lucena reported no adverse events after the use of Intracameral moxifloxacin¹⁸. A study conducted by Matsuura K et al in Japan looked for safety of Intracameral moxifloxacin and found it to be safe for prophylaxis of endophthalmitis¹⁹. Another study conducted by Koktekir looked for the safety of Intracameral moxifloxacin and found that there are no added risks to the patient who were given Intracameral moxifloxacin²⁰. Similar results were found in our study with no adverse reaction in either of the group receiving Intracameral antibiotics.

Despite the established effectiveness and safety of Intracameral antibiotics in the prophylaxis of endophthalmitis there is still no consensus on the use of Intracameral antibiotics for post op endophthalmitis prophylaxis²¹. Multiple reasons have been mentioned for the reluctance in the use of Intracameral antibiotics. The first concern is the changing infecting organism spectrum and sensitivity; hence, a periodic evaluation is mandatory. The second is the possibility of increasing resistance which is unlikely as a person will receive it only twice in his lifetime at the time of cataract surgeries²².

The price of cefuroxime is significantly less than moxifloxacin; therefore it is an attractive option for the prophylaxis of endophthalmitis in developing countries. Moxifloxacin can be reserved for more resistant infections.

CONCLUSION

The study reveals that Intracameral use of cefuroxime and moxifloxacin is effective in controlling post-operative endophthalmitis in rural Pakistan with high frequency of cataract surgeries without untoward side effects.

AUTHOR'S CONTRIBUTION

Shakeel A: Designed research methodology, Literature search, Data collection, Literature review, Manuscript writing

Ali SI: Conceived idea, Data interpretation, Manuscript final reading and approval

Sultan S: Statistical analysis, Manuscript writing, Literature search, Literature review

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Conflict of Interest: None.

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REFERENCES

- Barry P, Seal DV, Gettinby G, Lees F, Peterson M, Revie CW; ESCRS Endophthalmitis Study Group. ESCRS study of prophylaxis of post-operative endophthalmitis after cataract surgery: preliminary report of principal results from a European multicenter study. *J Cataract Refract Surg.* 2006; 32(3):407-410.
- Durand ML. Bacterial and Fungal Endophthalmitis. *Clin Microbiol Rev.* 2017; 30(3): 597-613
- Baig R, Mal PB, Ahmed K, Sadiq SN, Zafar S, Jabeen G, et al. Microbial Profile and antibiotic susceptibility trend in post-operative endophthalmitis. *J Pak Med Assoc.* 2019; 69(11): 1647-1650
- Nentwich MN, Ta CN, Kreutzer TC, Li B. Incidence of post-operative endophthalmitis from 1990 to 2009 using povidone iodine but no Intracameral antibiotics at a single academic institution. *J Cataract Refract Surg.* 2015; 41(1):58-66.
- Gentile RC, Shukla S, Shah M, Ritterband DC, Engelbert M, Davis A, et al. Microbiological spectrum and antibiotic sensitivity in endophthalmitis: A 25-year review. *Ophthalmology.* 2014;121(8):1634–1642
- Koroleva IA, Kozhukhov AA, Povidone Iodine in Ophthalmological Practice. *Clin Ophthalmol.* 2018; 18(1):45-49.
- Grzybowski A, Kanclerz P, William MG, The use of Povidone-iodine in ophthalmology, *Curr Opin Ophthalmol.* 2018; 29(1):19-32.
- Lin YH, Kang EYC, Hou CH, Huang YC, Antibiotic susceptibility profiles of ocular and nasal flora in patients undergoing cataract surgery in Taiwan: an observational and cross sectional study, *BMJ Open.* 2017 ;(8): 17352. doi: 10.1136/bmjopen-2017-017352.
- Espiritu CRG, Caparas, VL, Bolinao JG. Prophylactic Intracameral levofloxacin in cataract surgery- an evaluation of safety. *Clin Ophthalmol.* 2017; 11:2199-2204. doi: 10.2147/OPTH.S144625. eCollection 2017.
- Haripriya A, Chang DF, Nambur S, Smita A, Ravindran RD. Efficacy of Intracameral Moxifloxacin Endophthalmitis Prophylaxis at Aravind Eye Hospital. *Ophthalmology.* 2016; 123(2):302-308.
- Wade PD, Khan S, Khan MD. Endophthalmitis: Magnitude, Treatment, and Visual outcome in North West Frontier Province of Pakistan. *Ann Afr Med.* 2009; 8(1): 19-24
- Narsani AK, Nagdev PR, Lohana MK, Jatoti SM, Gilal I. Incidence and Visual Outcome of Acute Postoperative Endophthalmitis. *J Ayub Med Coll Abbottabad.* 2011; 23(2): 100-103
- Caravaca GR, Sáenz GMC, Campo VDMC, Alba AY, Puente AA. Incidence of endophthalmitis and impact of prophylaxis with cefuroxime on cataract surgery. *J Cataract Refract Surg.* 2013; 39(9) : 1399-1403
- Linertova R, Gonzalez RA, Perez LG, Plasencia MA, Dorta LMC, Reyes JAA, et al. Intracameral cefuroxime and moxifloxacin used as endophthalmitis prophylaxis after cataract surgery: systematic review of effectiveness and cost-effectiveness. *Clin Ophthalmol.* 2014; 8: 1515–1522. doi: 10.2147/OPTH.S59776
- Haripriya A, Chang DF, Ravindran RD. Endophthalmitis Reduction with Intracameral Moxifloxacin Prophylaxis, Analysis of 600 000 Surgeries .*Ophthalmology.* 2017; 124(6):768-775
- Gower EW, Lindsley K, Tulenko SE, Nanji AA, Leyngold I, McDonnell PJ. Perioperative antibiotics for prevention of acute endophthalmitis after cataract surgery. *Cochrane Database Syst Rev.* 2017; 13: 2. doi: 10.1002/14651858.CD006364.pub3.
- Daien V, Papinaud L, Gillies MC, Domerg C, Nagot N, Lacombe S, Daures JP, et al. Effectiveness and safety of an intracameral injection of cefuroxime for the prevention of endophthalmitis after cataract surgery with or without perioperative capsular rupture. *JAMA Ophthalmol.* 2016; 134(7):810–816
- Lucena NP, Pereira IMS, Gaete MIL, Ferreira KSA, Melega MV, Lira RPC, et al. Intracameral moxifloxacin after cataract surgery: a prospective study. *Arq Bras Oftalmol.* 2018; 81(2):92-94
- Matsuura K, Myushi T, Suto C, Akura J, Inoue Y. Efficacy and safety of prophylactic Intracameral moxifloxacin injection in Japan. *J Cataract Refract Surg.* 2013; 39 (11): 1702-1706
- Koktekir BE, Aslan BS. Safety of Prophylactic Intracameral Moxifloxacin Use in Cataract Surgery. *J Occul Pharmacol Ther.* 2012; 28(3): 278- 282
- Grzybowski A, Schwartz SG, Matsuura K, Rone OS, Arshinoff S, Ng JQ, et al. Endophthalmitis Prophylaxis in Cataract Surgery: Overview of Current Practice Patterns Around the World. *Curr Pharm Des.* 2017; 23(4):565-573
- Das T. Endophthalmitis Prophylaxis in cataract surgery. *Indian J Ophthalmol.* 2017; 65(12): 1277-1278