Original Article

Safety of Intrcameral Moxifloxacin Ophthalmic Solution for Antibacterial Prophylaxis in Cataract Surgery

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Purpose: To evaluate the safety profile of intracameral moxifloxacinin 0.5% ophthalmic solution in terms of anterior chamber (AC) reaction and endothelial toxicity.

Material and Methods: This prospective study was conducted in the department of Ophthalmology Fauji Foundation Hospital, Rawalpindi, from December 2006 to November 2007 and comprised of 200 patients. The patients were divided into two groups. Group 1 received 0.1 ml of intracameral moxifloxacin 0.5 % ophthalmic solution at the conclusion of the surgery and the patients in the group 2 were not given the intracameral antibiotic. None of the patients was given postoperative sub conjunctival antibiotic and steroid injection. All patients were examined for AC reaction and pachymetry was done preoperatively and postoperatively (first day, first week and 4 weeks postoperatively). Anterior chamber reaction and pachymetry values between the two groups were compared .Statistical analysis was done by using paired sample t test. P value of less than 0.05 was taken as significant.

Results: There was no statistically significant difference in corneal oedema (measured by pachymetry) between the two groups on the first postoperative day (p=624), and one month postoperatively (p=0.186). Anterior chamber reaction on the 1st postoperative day was not different in both groups (p=0.610). At 4 weeks there was no reaction in any patients and corneal thickness was also

restored to preoperative level.

Conclusion: Intracameral moxiloxacin 0.5% ophthalmic solution seems to be safe in terms of AC reaction and endothelial toxicity.

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Postoperative endophthalmitis is one of the most feared complications of cataract surgery as it seriously compromises vision. Although timely diagnosis and delivery of appropriate treatment do help in management[1], but in our set up the diagnosis is usually delayed as patients present late due to multiple reasons. It is in the last two decades that the prevelance of the staphylococcus epidermidis as a common cause of endophthalmitis has been recognized. The organisms which were previously considered to be harmless commensals are quite capable of causing endopthalmitis[2]. Multiple studies have been carried out to evaluate the bacterial contamination of anterior chamber fluid aspirates after surgery. Srinivasan R and collegues found 15% of AC aspirates to be positive for bacterial growth in which the staphylococci species was the commonest[3]. None of their patients developed infection as probably the inoculum size, host response, prophylactic antibiotics and improvement in the surgical technique have their role. Improvements in technique of surgery and prophylactic measures have had a beneficial effect, but despite this the incidence of endophthalmitis after cataract surgery has increased from 1994-2001 with reported incidence of 2.15 per 1000 cases[4]. Thus there still remains the need for protective antibiotics to combat the rise in the incidence of endophthalmitis and to treat the patients in a better way.

In addition to topical antibiotics many surgeons use intracameral antibiotics to prevent the infection. Among the antibiotics which are given intracameraly, most common are vancomycin and cefuroxime[5]. Although retrospective analysis suggest that there has been decrease in the risk of endophthalmitis with vancomycin [6]. Vancomycin has also been shown to increase the risk of cystoid macular oedema after cataract surgery[7]. Moreover, there are reports of emergence of resistant strains of many bacteria[8]. Because of all these facts the routine prophylactic use of vancomycin in cataract surgery is now discouraged worldwide[9]. Cefuroxime and cefazoline are two other medicines which are being used as intracameral antibiotics. The recent publication of ESCRS study has demonstrated that cefuroxime significantly decreases the risk for developing endophthalmitis after phacoemulsification cataract surgery[10]. Both of these as well as vancomycin are available as systemic preparations. They have to be reconstituted before delivery into the eye. Reconstitution of a drug increases the risk of toxic anterior segment syndrome (TASS).[11] TASS is an acute inflammation of anterior segment after cataract surgery. A variety of substances have been implicated including inappropriately reconstituted intraocular preparations. Incorrect PH and incorrect osmolality can also cause TASS. Another problem with vancomycin and cephalosporins is that they have time dependant efficacy. As the concentration of drug in AC decreases four times in first hour, so, this makes them a poor choice.

Considering the problems associated with the vancomycin and cephalosporins, the new antibiotic under consideration is moxifloxacin which is a forth generation fluoroquinolone. Forth generation quinolones have already surpassed the second generation as the antibiotics of choice in cataract surgery[12]. They have a wide spectrum of activity and they carry a lower risk of resistance developing against them. Moxifloxacin is available as self preserved ophthalmic solution. The self preserved nature of the medicine has led to its use as prophylactic intracameral injection. Fluoroquinolones are concentration dependant drugs. If they are put in AC in high enough dose they rapidly kill the bacteria. No special preparation is required for intracameral delivery, no millipore filter is needed and the syringe is easily identifiable by the faint yellow colour of the solution. Earlier studies had shown no toxicity with intracameral or intravitreal injection of Moxifloxacin in animal eye[13].

The aim of this study is to check the safety profile of 0.5% moifloxacin available as self preserved vigamox (Alcon) and, given as intracameral injection during cataract surgery.

MATERIAL AND METHODS

This case control comparative study was conducted at Fauji foundation hospital Rawalpindi from December

2006 to November 2007. 200 patients were enrolled for the study. 100 patients (cases) were injected with the medicine i.e intracameral moxifloxacin at the end of the surgery and they were put in group 1 whereas, 100 patients (controls) were operated in routine way and were placed in group 2. None of the patients were given sub conjunctival antibiotic and steroid injection at the end of the sugery. Patients with glaucoma, retinopathy, maculopathy, media opacity other than cataract, uveitis and corneal endothelial disease were not included in the study. Patients who suffered intra operative complications or those who had prolonged or difficult surgery were also excluded from the study.

Preoperative examination included uncorrected and corrected visual acuity, slit lamp examination, tonometry, fundoscopy and pachymetry. All patients were admitted one day prior to surgery. Biometry was done on the day of admition. On the day of surgery pupils were dilated with 1% tropicamide and 10% phenylephrine. Fifty two percent of surgeries were performed under local and 48% were done in topical anesthesia. Phacoemulsification was performed by single surgeon through 3.2 mm clear corneal incision and 5.25 mm PMMA IOL was implanted after enlarging the incision. No suture was applied in any case.

The prophylactic regime to reduce the risk of infection included topical 10% povidone-iodine on the periorbital skin, 5% povidone iodine in the conjunctival sac and eye lashes, drapping of the eyelashes and periorbital region, topical antibiotic drops one day prior to and on the day of surgery. At the start of the operating day a new bottle of moxifloxacin was opened and the contents of newly opened bottle were aspirated in 10 cc syringe by the operating assistant. 0.1 ml of 0.5 % pure moxifloxacin was aspirated in each of 1 cc tuberculin syringe before every case. The undiluted solution was injected in the anterior chamber at the end of the surgery. Postoperatively, for the infection control, the patients were given combination of topical 3 mg/ml tobramycin with 1 mg/ml dexamethasone every 2 hours along with systemic ciprofloxacin 500 mg twice daily for five days.

Patients were examined on the first postoperative day and further visits were scheduled at 1 week and 4 weeks interval. On each visit visual acuity was recorded, slitlamp examination was done for AC reaction. It was expressed as cells and flare and graded using hogan and kimura grading system. Pachymetry was done on each visit.

Data was entered and analysed using SPSS version 14. Student t-test was used to analyse the data. A p value of less than 0.05 was considered significant.

RESULTS

All patients completed the followup. Mean age of our patients in group 1 was 59 ± 6.22 (SD) and 58.75 ± 6.86 (SD) in group 2. All patients had variable corneal oedema on 1 st postoperative day as demonstrated by pachymetry. The mean preoperative pachymetry in group 1 was 519.56 ± 25.52 and group 2 was 517.30 ± 22.80. On first postoperative day it was 552.29 ± 26.26 in group 1 and 550.90 ± 21.30 in group 2. The difference in preoperative and postoperative 1st day pachymetry was significant in both groups (p=0.00). At one month, the pachymetry was 531.01 ± 26.76 group1 and 517.68 ± 21.87 in group 2. The difference between the preoperative and one month post operative corneal thickness was insignificant (p=0.32 and 0.672 respectively). Corneal thichness of two groups after 1st day and one month of surgery was almost the same, and the difference was found to be statistically insignificant (p=0.624 and p=0.186).

The difference in anterior chamber reaction in terms of cells and flare in both groups is insignificant (p=0.610 for cells and p=0.566 for flare) on the first postoperative day. At final visit there was no reaction in any patients.

Table 1: Corneal thickness observed by pachymetry (in micrometers) (n=100)

Means and Standard Deviation				
	Group 1		**Group 2**	
	Mean	SD	Mean	SD
Pre operative	519.56	25.52	517.30	22.80
Post operative 1st day	552.29	26.26	550.90	21.30
Post operative 1 month	521.01	26.78	517.68	21.87

Table 2: Anterior chamber reaction observed as cells and flare (n=100)

Means and Standard Deviation		
	Group 1	Group 2

	Mean	SD	Mean	SD
Cells	1.97	0.76	1.92	0.74
Flare	1.34	0.59	1.33	0.57

Table 3: Paired sample t test (n=100)

Means, Standard Deviation and Significance			
Group-1 verses Group-2	Mean	SD	Significance
Post operative corneal thickness (1st day)	1.390	28.26	0.624
Post operative corneal thickness (1 month)	4.080	30.64	0.186
Cells	0.050	0.978	0.610
Flare	0.010	0.174	0.566

DISCUSSION

The first report of successful prophylactic intracameral antibiotic injection was published in 1977[14]. It did not recieve significant attention and despite of the efficacy of this technique it was not considered until 2002 when Montan et al published their report in which they described a decreased rate of postoperative endophthalmitis with intracameral injection of 1 mg of cefuroxime[15].

Of the prophylactic methods for cataract surgery only povidone iodine is recommended[16]. If applied alone it reduces conjunctival flora by 91% for colony forming and 51% for species. If it is used along with topical antibiotic, it produces synergistic effect and leads to sterilization of 83% of the eye[17]. Despite its efficacy the rate of endophthalmitis increased after 1994. So, there was a need for protective antibiotic to check this rise in the rate of endophthalmitis. Topical antibiotics which gained popularity in the last few years for infection prophylaxis after cataract surgery were fluoroquinolones. In 2002 survey of the members of American Society of Cataract and Refractive surgery. Leaning noted that 86% of respondents were using second generation fluoroquinolones[18], whereas in a 2003 survey, only 21% were using second generation and 61% were using forth generation fluoroquinolones[19]. The reason for this change was increasing resistance towards the second generation drugs. Kowalski et al reported in 2001 that none of the staphlococcus aureus isolated from endophthalmitis isolates were sensitive to second generation fluoroquinolones[20]. These problems led to the development of forth generation antibiotics. These antibiotics have got a wider spectrum of activity against gram positive organisms which are the most common pathogens causing endopthalmitis. In addition they have a good coverage against gram negative organisms and anaerobes[12]. Moxifloxacin is found to be superior in terms of potency to gatifloxacin[21]. It seems to be a better choice as a prophylactic antibiotic as it has got lowest minimal inhibitory concentration (MIC). Mather et al did a retrospective study of 93 bacterial endophthalmitis isolates. He found that the MIC levels for Moxifloxacin ranged form 0.06-0.19 mg/ml[12]. Lindsay has shown in his study that Moxifloxacin has good aqueous penetration when given four times a day starting two days prior to surgery and that its concentration exceeds MIC levels for most common pathogens[22]. This shows that moxifloxacin can be an effective prophylavtic antibiotic even given through topical route. But, another important consideration is prevention of development of resistant strains which may develop with prophylactic use of an antibiotic. The drug level at which the development of resistant strains can be prevented is called mutation prevention concentration (MPC). It is another parameter of evaluation of potency of an antibiotic. Frequent and suboptimal use of an antibiotic increases the risk of development of resistant mutants. The MPC of fluoroquinolones is 8-10 times their MIC[23]. Achieving concentrations higher than this almost ensures the prevention of mutation. With topical use the aqueous concentration of Moxifloxacin levels or slightly exceeds its MPC, whereas with intracameral injection it achieves and ensures much higher concentration than its MPC (0.38 - 2.16mg/ml). We injected 0.1 ml of pure vigamox 0.5% ophthalmic solution without dilution in the AC at the end of the surgery. This is equilant to 0.5 mg of moxifloxacin. Bolinao and his collegues used the same concentration and calculated the concentration of Moxifloxacin in AC to be 952 mg/ml, which is 300 times its MIC and atleast 30 times its MPC[23].

Our concern was to check the effect of intracameral Moxifloxacin on cornea for which we examined the cornea clinically for striate and quantitatively by performing pachymetry before and after surgery. The other concern was effect of Moxifloxacin on blood aqueous barrier and whether it causes inflammation or not. The patients were

examined for aqueous flare and cells on the first post operative day and on the scheduled visits. The patients were followed for four weeks because in previous studies it has been suggested that wound healing is complete in four weeks and preoperative corneal thickness is also restored in four weeks. Moreover as the eye is usually quiet and the patients have no problem after that time, we loose follow up mostly after 4-6 weeks of surgery.

We found that the patients who were injected with intracameral Moxifloxacin had almost the same AC reaction as controls and that the corneal thickness that occurred after the surgery was not significantly different in two groups. Corneal thickness was restored to the pre operative levels and there was no sign of inflammation in AC at four weeks of surgery. This suggests that intracameral Moxifloxacin is not toxic to endothelium and it does not cause significant inflammation. The results of our study are supported by Espiratu et al who used the same concentration of intracameral moxifloxacin[23]. Sleve A.Arshinoff has also recommended the routine use of intracameral Moxifloxacin although he has used much lesser concentration of the antibiotic in AC[24].

CONCLUSION

Intracameral Moxifloxacin 0.5% ophthalmic solution appears to be non toxic to eye in terms of AC reaction and endothelial damage.

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