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Evaluating the therapeutic response of intra-vitreal moxifloxacin in acute post-operative (cataract) endophthalmitis.

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ABSTRACT… Objective: To assess the effectiveness and side effects of injecting intra-vitreal moxifloxacin (IV-M) in the treatment of acute post–operative (cataract) endophthalmitis having visual acuity ≥ hand movements. **Study Design:** Prospective, Interventional Case Series study. **Setting:** Eye Department of Qazi Hussain Ahmad Medical Complex, Nowshera. **Period:** 2018 to Jan. 2021. **Material & Methods:** Thirty (30) patients with post–op endophthalmitis who presented within 4 weeks with visual acuity (VA) ≥ hand movements (HM) received two IV-M injection at 24 hr. interval at an Eye department. Patients with prior history of ocular diseases or intra-vitreals were excluded. Patients were followed up to 12 weeks either for improvement or deterioration of endophthalmitis. No. of patients who attained VA ≥ 6/12 and 6/60 at the 12th week visit were compared with the no. of patients at presentation, by performing statistical analysis. In addition, pre-therapy VA converted into logarithm of minimum angle of resolution (Log MAR) at the time of presentation was compared with post-therapy VA at end of 12th week by using repeated measure ANOVA test. **Results:** Twenty five (83.3%) patients completely resolved while two patients underwent core vitrectomy. 14 (46.66%) and 22 (73.34%) patients achieved VA ≥ 6/12 and 6/60, respectively at 12th week visit as compared to 04 (13.33%) and 08 (26.66%) patients respectively at the time of presentation ($p = 0.043$). In the same way, mean Log MAR VA pre-intervention was 0.811 which improved to 0.344 at the 12th week ($P < 0.05$). We didn't observe any toxicity to IV-M. **Conclusion:** Intra-vitreal moxifloxacin was efficacious and safe in the treatment of post-operative (cataract) endophthalmitis.

Key words: Cataract, Endophthalmitis, Moxifloxacin, Intra-vitreal.

INTRODUCTION

Endophthalmitis is one of the most fearful infective outcome of the cataract extraction which causes irreversible visual loss in most of the cases. It is estimated to be at 0.13% post-operatively.[1] Various factors are implicated in the causation of acute post-operative (cataract) endophthalmitis including type of incision, technique of surgical procedure, posterior capsule rent, vitreous loss, perioperative complications, adnexal diseases, and diabetes.[2] Intra-vitreal antimicrobials with or with-out core vitrectomy (CV) is the definitive treatment for this dreadful condition. The Endophthalmitis Vitrectomy Study (EVS) evaluated the results of early vitrectomy vs. vitreous tap in those having acute post-operative endophthalmitis and observed that patients having initial visual acuity (VA) ≥ hand movement (HM), no difference in visual outcome whether or not an early vitrectomy was performed. However, in patients with initial light perception (LP) only vision, early vitrectomy resulted in threefold increase in the frequency of attaining ≥ 6/12 VA and a 50% reduction in the frequency of severe visual loss as compared with a vitreous tap.[3]

In current practice, intra-vitreal ceftazidime (IV-C) 2 mg/0.1cc and vancomycin (IV-V) 1 mg/0.1cc are used to manage post-operative endophthalmitis.[4] IV-V use is associated with hemorrhagic occlusive retinal vasculitis (HORV), dreadful sight-threatening toxicity of the drug, with poor prognosis.[5] One of the major concern in the management of post-operative endophthalmitis

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is the emergence of vancomycin resistant strains causing devastating sight threatening endophthalmitis.[6]

The efficacy of using intra-cameral moxifloxacin (IV-M) as a prophylactic measure against pos-operative (cataract) endophthalmitis has been explored in some trials.[7] It was observed that intra-cameral moxifloxacin decreased endophthalmitis rates with minimum or no toxicity at standard doses. In the same way two other studies revealed the effectiveness of intra-cameral moxifloxacin as a prophylactic agent against post-operative endophthalmitis.[8,9] Another study, has found out the efficacy and safety of trans-zonular injection of moxifloxacin plus corticosteroids and vancomycin into the vitreous cavity in decreasing post-operative inflammatory reaction.[10]

Additionally, IV-M injections were proven effective in the treatment of post-traumatic endophthalmitis caused by resistant Gram –ve microbes.[11] Similarly, IV-M was also found to be successful in the treatment of post-traumatic endophthalmitis after open globe injury.[12] However, safety and efficacy of IV-M in the management of post-operative (cataract) endophthalmitis is not extensively explored and this was the rationale behind conducting this study to explore its beneficial and adverse effects as compare to conventional intra-vitreal regimen of vancomycin and ceftazidime combination in endophthalmitis.

MATERIAL & METHODS

This was a prospective, interventional case series study. The trial comprised of 30 patients who presented with post Phacoemulsification endophthalmitis between Jan. 2018 to Jan. 2021 at an Eye Dept. of Qazi Hussain Ahmad Medical Complex (0358/R&D/IERB/NMC), Nowshera. The study was granted approval from the institutional ethical review board (IERB). All patients suffered from infection within 4 weeks of surgery, with VA ≥ HM and no previous ocular ailments (glaucomatous eyes, retinal pathologies and other intraocular procedures) were enrolled in the trial. Those who were given intra-vitreals or underwent CV for endophthalmitis with VA < HM were expelled from the trial along with those patients who were unwilling for participation.

After thorough clinical history, patients underwent detailed ophthalmic assessment in the form visual acuity (VA), intraocular pressure (IOP), slit lamp examination (SLE), fundus examination by indirect ophthalmoscopy (if possible) and B-scan U/S.

Subjects were briefed about the possible side effects of injection and written informed consent were taken from everyone. All subjects received two IV-M injections 24hr apart. The IV-M were injected in the mini operative procedure room under aseptic environment. Before intra-vitreals, 5% povidone-iodine drops were instilled in the lower conjunctival fornix and topical anesthetic 1% proparacain drops were instilled twice at 5min. intervals. Lid speculum was inserted before injection to avoid needle contact with lashes or lid margins.

Vitreous sample was taken by using 26G needle attached with 1cc syringe, 4mm away from limbus, and approx. 0.2cc of vitreous was aspirated. 0.5mg/0.1cc of moxifloxacin was aspirated directly from 0.5% moxifloxacin preservative-free ophthalmic drops (Moxigan 0.5%, Allergan Ins. USA) with the help of 1cc D/S and injected intra-vitreally with 27G needle via the par-plana about 4mm away from limbus.

Vitreous tap was sent to the lab for microscopy and culture and sensitivity testing for different bacteria and fungi. In the microbiology lab. Gram and KOH staining was performed for identification of different bacteria and fungi respectively. Vitreous tap samples were then inoculated on blood agar and Mac Conkey agar for bacterial culture and on Sabouraud Dextrose Agar for fungal culture. Anti-microbial susceptibility testing was undertaken by the disc diffusion technique.

All eyes were assessed on day 1st, 3rd, 5th, 1st week, 4th week, 8th week and 12th week of 2nd intra-vitreal injection. Eyes were examined for signs of resolution of endophthalmitis which included complete absence of inflammatory activity in anterior and posteriors segment. We calculated

the no. of eyes that showed full recovery with nil infectivity and eyes that required CV. We assessed VA in all eyes at every follow up and no. of eyes that attained VA ≥ 6/12 and 6/60 at 12th week was computed and compared with the no. of eyes at baseline for statistical analysis.

Similarly, pre-treatment Log MAR VA was compared with post-treatment VA by the end of 12th week with repeated measure ANOVA test. Results were considered statistically significant if the $p < 0.05$. Statistical analysis was done with the help of SPSS version 26.0 (IBM Corp. USA).

Addionally, patients were also assessed for signs of hyper-sensitivity reactions to intra-vitreal moxifloxacin, i.e. retinal vasculitis or aggravation of AC reaction or vitritis after the injection.

RESULTS

Thirty eyes of 30 subjects were recruited in the trial. The mean age (±SD) of subjects were 60.14 ±7.95 yrs. Male/female ratio was 1.32. The mean (±SD) time of presentation of Endophthalmitis was 9.5 ± 6.44 days (as shown in Table-I). Table-II depicts the clinical features of eyes at the time of presentation.

We explored diabetes as the commonest cause for post-operative endophthalmitis in our study (Table-III). 18 (60%) of patients were diabetics and were taking medications for their condition. All the subjects were having normal fasting glucose level at the day of surgery.

We assessed the eyes up to 12th week after IV-M and 25 of 30 (83.33%) subjects completely resolved however, two required vitrectomies, for persistent infection. In the 1st patient's eye vitrectomy was performed for persistent infectivity. Haemophilus Influenzae was cultured from the agar plate inoculated with the vitreous specimen, though the sensitivity of the microbe to moxifloxacin in vitro was good but as we did not observe the efficacy of drug in clinical scenario of the above patient, so we injected IV-C and IV-V at the end of CV in that patient for optimal response. In the 2nd eye we also performed CV for persistent infectivity, however culture yielded no growth from the vitreous sample, and IV-C and IV-V were injected at the end of procedure.

Prior to IV-M, four (13.33%) eyes had VA ≥ 6/12 as compared to 18 (60%) eyes at 12th week post-treatment ($p < 0.043$). Similarly, 8 (26.66%) eyes had VA ≥ 6/60 pre-intervention which increased to 22 (73.33%) eyes at 12th week post-intervention ($p < 0.05$). Figure-1 compares the no. of eyes before IV-M vs. 12th week post-intervention at different levels of VA. In addition, mean ±SD Log MAR VA before IV-M was 0.811 ± 0.501 which improved to 0.344 ± 0.286 at 12th week following injection ($p < 0.05$).

We didn't observe any toxicity to the drug in the form of occlusive retinitis and intra-ocular inflammatory reactions after injecting it intra-vitreally.

Culture result was +ve in 17 of 30 (56.66%) cases (Table-IV). The most common micro-organisms were Gram +ve bacterial pathogens, mostly coagulase -ve staphylococci. Antibiotic sensitivity testing revealed that 100% of bacterial isolates were sensitive to moxifloxacin.

Pre-treatment Characteristics	Values
No. of eyes	30
Mean ± SD Age (yrs.)	60.14 ±7.95
Males	7 (23.3%)
Females	23 (66.7%)
Mean ± SD, Time of presentation	9.5 ± 6.44 days
Mean ± SD, Log MAR VA at presentation	0.811 ± 0.501

Table-I. Patients demographics

Clinical Features	No. of Patients
Pus in anterior chamber (Hypopyon)	10 (33.33%)
Moderately visible retinal vessels	06 (20%)
Faintly visible retinal vessels	23 (76.66%)
No, red reflex	07 (23.33%)
Detached Retina	0 (0%)

Table-II. Clinical signs present in eyes.

Risk Factors	No. of Patients
DM	18 (60%)
PCR	06(20%)
Other Surgical events	03(10%)
Corneal incision leaks	02 (6.66%)
Dacryocystitis	01 (3.33%)

Table-III. Risk factors for endophthalmitis. DM= diabetes mellitus, PCR= posterior capsular rent

	No. of Vitreous Specimens	Antibiotic Sensitivities	(no. of Vitreous Specimens)		
		Moxifloxacin	Vancocin	Fortum	Gentacin
Gram +ve					
Staphy. epidermides	15	15	12	08	N/T
Strept. pneumoniae	04	04	02	01	N/T
Staphy. aureus	02	02	01	01	N/T
Gram -ve					
Haemophilus	01	01	N/T	01	01
No, yield	07	N/A	N/A	N/A	N/A

Table-IV. Microbiology lab results of culture and sensitivity for vitreous samples
N/T= Not tested, N/A= Not Available, Fortum= ceftazidime

DISCUSSION

One of the dreadful and horrible complication after cataract procedure is the development of Endophthalmitis which if not timely managed can lead to irreversible loss of vision and eye.[14] Post-operative (cataract) acute endophthalmitis incidence is reducing with the passage of time due to improved aseptic measures in the OT and disposable items used in the surgery, it was nearly 0.24% in the 1st decade of this century, 0.09% in the 90s, 0.16% in the 80s and 0.33% during the 70s.[1] Incision technique, no use of intra-cameral antibiotics (prophylactically), extra-capsular or intra-capsular cataract extractions, posterior capsular rent, silicon intra-ocular lenses, intra-operative complications were found to be strongly associated with acute endophthalmitis.[2] Endophthalmitis is treated with intra-vitreal antibiotics along with vitreous tap or vitrectomy. Although EVS used intra-vitreal vancomycin 1mg and amikacin 0.4mg, but today intra-vitreal ceftazidime 2mg/0.1cc along with vancomycin 1 mg/0.1cc is most commonly used in cases of acute post-operative (cataract) endophthalmitis.[3,4] However, IV-V is associated with HORV, a hyper acute inflammatory reaction to the drug (vancomycin) causing pan-ocular inflammation with hemorrhagic retinitis and ischemic retinal necrosis secondary to occlusive retinitis. HORV is basically an exaggerated immune response to vancomycin with dismal prognosis, as > 70% eyes develop VA ≤ 6/60 and 30 % with no LP. Neovascular glaucoma develops in > 50% of the eyes.[5]

Gram +ve bacteria are mostly involved in the causation of post-operative (cataract) endophthalmitis.[15] In the current clinical practice IV-V is used for treatment of endophthalmitis caused by Gram +ve bacteria. But, unfortunately some strains are emerging with decreased sensitivity and more resistance against the vancomycin, leading to worst prognosis in these cases.[6]

IV-M has also shown to be safe in experimental animal trials with negligible changes in electroretinogram or histological specimens of retinal tissues.[13] Some studies and case reports in humans have also demonstrated the safety and efficacy of intra-vitreal moxifloxacin, especially in post-traumatic endophthalmitis.[11,12]

Our study showed the efficacy of IV-M in patients with post-op (cataract) endophthalmitis presenting within 4 weeks of surgery and with VA ≥ HM. 83.33% of eyes in our trial resolved with two intra-vitreal injections. In comparison with other studies, the safety profile of IV-M was excellent as we didn't observe any case of hyper-sensitivity to the moxifloxacin.

Numerous researchers have proven that majority of cases of endophthalmitis are caused by Gram +ve bacteria which are coagulase –ve, similar to the findings of our study.[3] Similarly another study reported that the bacteria mostly responsible for post-operative (cataract) endophthalmitis are extremely responsive to moxifloxacin, supporting our study findings.[16]

The main short coming of our study was the

limited sample size, lack of control group with masking effect and inclusion of only post-operative cataract endophthalmitis with VA ≥ HM. Additionally, we conducted the study at our hospital in the Eye dept. showing results at our setup which may be different from other centers depending upon various factors, in order to explore further we need multicenter studies with larger sample size to determine about the effectiveness and safety of this novel drug and adopting this new clinical practice. Furthermore more studies need to be conducted to establish the appropriate dosing, frequency and no. of injections needed for resolution of post-cataract surgery endophthalmitis.

CONCLUSION

Intra-vitreal moxifloxacin was efficacious and safe in the treatment of post-operative (cataract) endophthalmitis.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Adnan Ahmad	Study concept, design, data collection, data analysis, drafting.	
2	Mubbashir Rehman	Data collection, analysis, literature review, critical review.