Original Article

Comparison of Role of Pre Injection Topical Antibiotic and Per Operative One Drop of 5% Povidone-iodine in Conjunctival Sac, Before Giving Intra-vitreal Injection of Anti-VEGF, in Prevention Against Acute Endophthalmitis

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Objective: To compare the role of topical antibiotic course, 4 hourly for 1 day before intra-vitreal injection of Anti-VEGF and per-op one drop of 5% povidone-iodine solution in conjunctival sac just before injection, in prevention against endophthalmitis.

Study Design: Randomized Controlled Trial

Study: Ophthalmology Department, DHQ Teaching Hospital, Gujranwala and Major Eye Clinic Centre, Gujranwala from January 2018, to June, 2019.

Methodology: This trial was carried out on a total of 802 eyes for the duration of one and a half year. Patients presenting with indications for Intra-vitreal injection of Anti-VEGF to Eye OPD were included in the study. Patients were divided into two groups. Group-A401 eyes who received only one drop of 5% povidone-iodine solution in conjunctival sac just before intra-vitreal injection and Group-B 401 eyes did course of topical antibiotic (Moxifloxacin) for one day, before intra-vitreal injection of Anti-VEGF.

Results: In group-A, there were 230(57.5%) were females and 171(42.5%) were males. In group-B, 240(60.0%) were females and 161(40.0%) were males. In group-A, no case of endophthalmitis was reported 0(0.00%) and in group-B as well 0(0.00%).

Conclusion: A drop of 5% povidone-iodine in conjunctival sac is sufficient to prevent against endophthalmitis. There is no role of Topical antibiotic (Moxifloxacin) before intra-vitreal injections in the prevention against acute endophthalmitis.

Keywords: Topical Antibiotic, 5% Povidone-Iodine, Avastin (Bevacizumab), Acute Endophthalmitis, Intravitreal Anti-VEGF.

Introduction:

Retinal hypoxia caused by any clinical condition results in the formation and release of vascular endothelial growth factor (VEGF).[1] This can in turn result in formation of abnormal blood vessels at aberrant sites causing complications like intraocular hemorrhage and its sequelae. Ocular angiogenesis is a cause of severe worldwide visual loss and ocular morbidity.[2]

Bevacizumab (Avastin), Ranibizumab (Patizra/Lucentis) and Eylea (Aflibercept) are commercially available Anti-VEGF's. These are recombinant humanized monoclonal IgG1 antibodies that binds to and inhibits vascular endothelial growth factor (VEGF), reducing the growth of new blood vessels. The development of anti-vascular endothelial growth factors (anti-VEGF) has revolutionized the treatment of a plethora of ocular angiogenic disease processes.[3]

It has become the favored therapy for conditions such as choroidal neovascularization, diabetic macula edema, vein occlusions, myopic choroidal neovascularization, and retinopathy of prematurity.[4]

Anti-VEGFs are typically given by transconjunctival intravitreal injections into the posterior segment. The typical dose is in 0.05ml in adults. The risk of serious vision-threatening complications with intra-vitreal injections is quite low, and adherence to good technique reduces this risk even further.[5]

Endophthalmitis is a dreadful complication following intra-vitreal injection of Anti-VEGF. Prophylactic pre-injection and post-injection antibiotics are frequently used in order to reduce the likelihood of endophthalmitis; however, while prophylactic antibiotics may reduce ocular flora, povidone-iodine prep is considered more effective according literature.[6,7]

In this study, we intended to compare the role of Pre-Intravitreal injection, topical antibiotic for one day before injection and per-op one drop of 5% povidone- iodine solution in conjunctival sac just before injection, in prevention against acute endophthalmitis. Study population was the patients presenting with indications for intra-vitreal Anti-VEGF to Eye OPD, Department of Ophthalmology, Gujranwala Medical College/DHQ teaching Hospital, Gujranwala and Major Eye Clinic Centre, Gujranwala.

Materials and Methods:

This trial was carried out on a total of 802 eyes for the duration of one and a half year. Patients presenting with indications for Intra-vitrealanti-VEGF to Eye OPD were included in the study. Patients were divided into two groups.

Group-A 401 eyes who received one drop of 5% povidone-iodine solution in conjunctival sac just before intra-vitreal injection of anti-VEGF and **Group-B** 401 eyes did course of topical antibiotic (Moxifloxacin) for one day, before intra-vitreal injection.

Patients with active infection of the ocular adnexa (blepharitis, meibomitis) or a blocked nasolacrimal duct/positive regurgitation test are at high risk for endophthalmitis were excluded from the study.

Before prescribing Intravitreal injection of Anti-VEGF all the patients underwent thorough fundus Examination. After papillary dilatation, fundus examination was carried out with90 diopter (D) lens. Peripheral retinal evaluation was performed using indirect ophthalmoscope and, where indicated, ultrasonography (B- scan) was performed. OCT macula was done to estimate the pre-injection macular thickness and to rule out any vitero-macular traction or fibrotic bands.

In group-A patients before intravitreal injection, only 5% povidone - iodine was instilled in the conjunctival sac with no use of topical antibiotic before injection. In group-B, topical antibiotic (Moxifloxacin) four hourly, was used for one day, a day before injection.

All injections were given in operation theatre. A solution of 10% povidone-iodine was used for disinfection of forehead, eyelids and eyelashes. After draping the patient with a sterilized sheet, wire lid speculum was applied for lid control. Before injection, topical 5% povidone-iodine solution and topical 0.5% proparacaine drops were installed in conjunctival sac in both the groups.

The Anti-VEGF injection, supplied in 1.0ml tuberculin syringe, was used. Two commercially available Anti- VEGFs (ranibizumab and bevacizumab) were used as per bought by the patients. Bevacizumab (Avastin) is cost effective than Ranibizumab (Patizra). In our study bevacizumab(Avasin) was used in more than 95% of the patients. Intraviteral injection was given 3.5 mm or 4.00 mm away from limbus depending upon the status of lens.

After injection, 5%povidone - iodine was again instilled in conjunctival sac in both the groups. IOP was checked digitally.

Follow up of the patients was after 12 hours, 14days and 2 months days to see any signs of endophthalmitis or any other complications.

Results:

During 18 months from January 2018, to June, 2019,this trial was carried out on a total of 802eyes. Patients were divided into two groups. **Group-A**401 eyes who received just one drop of 5% povidone-iodine solution in conjunctival sac before intra-vitrealinjection and **Group-B**402 eyes did course of topical antibiotic (Moxifloxacin) before intra-vitrealinjection.

In group-A, there were 230(57.5%) were females and 171(42.5%) were males. In group-B, 240(60.0%) were females and 161(40.0%) weremales (Table-1). The mean age of patients in group-A was 57.3±12.6 years and in group-B was 56.1±11.2 years.

In group-A, there were 36(9.0%) in 30-45 years age group, while 124(31.0%) and 240(60.0%) were in 46-60 years and >60 years age groups respectively. In group-B, there were50(12.5%) in 30-45 years age group, while 161(40.0%) and 190(47.5%) were in 46-60 years and >60 years age groups respectively (Table 2).

In group-A, there were 240(60.0%) who were diagnosed Diabetic Maculopathy, while 50 (12.5%), 20 (5.0%), 50 (12.5%), 20 (5.0%) and 21 (5.0%) patients were diagnosed as Proliferative Diabetic Retinopathy (PDR), Age Related Macular Degeneration (ARMD), Central Retinal Vein Occlusion (CRVO), Branch Retinal Vein Occlusion (BRVO), Diabetic Vitreous Hemorrhage respectively.

In group-B, there were 231(57.5%) who were diagnosed Diabetic Maculopathy, while 44(11.0%), 26(6.5%), 46(11.5%), 32(8.0%) and 22(5.5%) patients were diagnosed as Proliferative Diabetic Retinopathy (PDR), Age Related Macular Degeneration (ARMD), Central Retinal Vein Occlusion (CRVO), Branch Retinal Vein Occlusion (BRVO), Diabetic Vitreous Hemorrhage. (Table 3)

In group-A, there were 22(5.5%) who had Subconjunctival Hemorrhage, while 16(4.0%) patients in group-B.In group-A, there were 6(1.5%) who had Corneal Abrasion, while 3(0.75%) patients in group-B.

In group-A, there were 8(2.0%) who had Congestion at injection site, while 7(1.75%) patients in group-B.In group-A, Endophthalmitis was not present 0(0.00%) and in group-B as well 0(0.00%). (Table 4).

Table-1: Comparison of gender distribution between groups

Gender	Groups		Total
	Group-A (only 5% pyodine-iodine solution)	Group-B (Topical Antibiotic (Moxifloxacin)	
Female	230	240	401
	57.5%	60.0%	58.75%
Males	171	161	401
	42.5%	40.0%	41.25%
Total	200	200	802
	100.0%	100.0%	100.0%

Table-2: Comparison of age groups distribution between groups

Age groups	Groups		Total
	Group-A (5% pyodine-iodine solution)	Group-B (Topical antibiotic (Moxifloxacin)	
30-45 years	36	50	86
	9.0%	12.5%	10.75%
46-60 years	124	161	284
	31.0%	40.0%	35.50%
>60 years	240	190	431
	60.0%	47.5%	53.75%
Total	401	401	802
	100.0%	100.0%	100.0%

Table-3: Comparison of diagnosis between groups

Diagnosis	Groups	
	Group-A (5% pyodine-iodine solution)	Group-B (Topical antibiotic (Moxifloxacin)
Diabetic Maculopathy (DM)	240	231
	60.0%	57.5%
Proliferative Diabetic Retinopathy (PDR)	50	44
	12.5%	11.0%
Age Related Macular Degeneration (ARMD)	20	26
	5.0%	6.5%
Central Retinal Vein Occlusion (CRVO)	50	46
	12.5%	11.5%
Branch Retinal Vein Occlusion (BRVO)	20	32
	5.0%	8.0%
Diabetic Vitreous Hemorrhage	21	22
	5.0%	5.5%

Table-4: Comparison of complications between groups

Complications	Groups		p-value
	Group-A (5% pyodine-iodine solution)	Group-B (Topical antibiotic (Moxifloxacin)	
Subconjunctival Hemorrhage	22	16	0.127
	5.5%	4.0%	
Glaucoma	13	12	0.534
	3.25%	3.0%	
Corneal Abrasion	6	3	0.175
	1.5%	0.75%	
Congestion at injection site	8	7	0.312
	2.0%	1.75%	
Endophthalmitis	0	0	0.921
	0.00%	0.00%	

Discussion:

This is an on-going study. Till now, no case of endophthalmitis has been reported. Incidence of

endophthalmitis ranges from 0.019% to 2.5%.[8-11] Increasing sample size, involving more eye care centres and including data of intravitreal injections of coming years can help us to report the incidence of endophthalmitis in our setting.

In this study, all the surgeons used to wear facemask and followed strict sterilization regime while giving intravitreal injections.The most important aspect that an ophthalmologist should consider while giving intravitreal injections is the selection of patients and precautions taken during injection.

The use of 5% povidone–iodine in the conjunctival sac is an accepted universal practice and is a strong recommendation for preventing endophthalmitis.[12] In our study use of 5% povidone-iodine was made sure before and after injection in both the groups, as recommended by international guidelines for giving intraviteal injections. This can be one of the reasons why no case of endophthalmitis was reported in this study.

It has become a universal trend to use pre-injection topical antibiotics assuming that their use reduces the risk of infection; however, there is evidence disputing this assumption[10] and none has shown reductions in the incidence of post procedure endophthalmitis.[13] In this study pre-injection topical antibiotics course was completed by patients of one group (Group B) and it was compared with other group (Group A) who had not used topical antibiotics and only 5% povidone-iodine was used just before the injection and there was no difference found in both the groups.

Moxifloxacin, ofloxacin and trimethoprim/ polymyxin-B antibiotics are used for the treatment of ocular surface infections. The use of topical antibiotics, pre and post operatively in cataract surgery, is the norm followed around the world. In this intraocular procedure patients are given antibiotics may be once in their life.

In contrast, patients with wet Age Related Macular Degeneration (ARMD) receive topical antibiotics for years on regular intervals after each intravitreal injection.[9,16] Thus repeated use of antibiotics has the potential to develop resistant bacteria strains.[13] That is why fluoroquinolone resistance is an emerging problem in ocular microbiology.[17-20]

Recently, Kessel L et al in an analysis, found no evidence that topical fluoroquinolone antibiotics can prevent endophthamitis.[15] In this study; It was found that use of pre-injection topical antibiotic was of no use and injudicious.

Conclusion:

A drop of 5% povidone-iodine in conjunctival sac is sufficient to prevent against endophthalmitis. There is no advantage of topical antibiotic (Moxifloxacin) before intravitreal injections in the prevention of endophthalmitis.

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