

# Role of Post-injection Antibiotics after Intravitreal Bevacizumab Injection in Preventing Endophthalmitis

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**Purpose:** To evaluate the role of using antibiotics after intravitreal injection of Bevacizumab in patients to prevent postinjection endophthalmitis.

**Material and Methods:** A multicentre prospective case control study was carried out at PUMHSW Hospital Nawabshah and Ghulam Muhammad Mehar Medical college Hospital Sukkur. The injection was given by different surgeons but with same technique. Immediately after intravitreal Bevacizumab injection the patient was started with Topical Moxifloxacin and oral ciprofloxacin 500 mg for three days. Patients were followed at 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> week post-injection to look for any sign of endophthalmitis.

**Result:** Out of 620 injections given in 480 eyes, 310 were control group without any post-injection medicine and 310 were cases who were given post-injection medicine. No case of proven or suspected endophthalmitis was identified, corresponding to a risk of 0% per injection.

**Conclusion:** In our study use of antibiotics after intravitreal Bevacizumab injection does not make any difference for the prevention of postoperative endophthalmitis.

**Keywords:** Endophthalmitis, Bevacizumab, Intravitreal Antibiotics.

With the recent advancement of widespread indications for the use of antivascular growth factor for different retinal disorders like wet ARMD, Diabetic maculopathy, and CRVO, the frequency of intravitreal injection of these drugs is rising.

In the year 2009 more than 1000,000 intravitreal Anti VEGF injections were performed in the united states alone.<sup>1</sup> The number of intravitreal injection of anti VEGF given for different indications has increased so much so that it is now 2<sup>nd</sup> most to cataract surgery in European countries.<sup>2</sup>

The documented complications of the therapy are bacterial endophthalmitis, sterile Uveitis, traumatic cataract and rhegmetogenous retinal detachment.<sup>3</sup> However none of the adverse events exceeded 0.21%.<sup>4</sup> Endophthalmitis is a visual threatening inflammatory disorder resulting from infection of vitreous cavity. Intravitreal injection, penetrating trauma and intraocular surgery are the routes through which exogenous endophthalmitis may occur.<sup>5</sup> Multicentre clinical trials with Anti VEGF therapy showed an incidence rate of Post injection Endophthalmitis by

0.019% – 1.6%.<sup>6-8</sup>

Recent survey have suggested that 40% of retina specialists use topical antibiotics prior to intravitreal antiVEGF injection and 86% use topical antibiotics after intravitreal anti VEGF injection.<sup>9</sup> One of the study<sup>10</sup> showed 3 cases of endophthalmitis postinjection to Ranibizumab out of 1276 cases who were not given antibiotics before or after injection.

Because of reported cases of Endophthalmitis we carried out a study to reveal the role of post injection antibiotics for it's prevention, keeping the standard international protocol of preoperative and operative care during intravitreal Bevacizumab injection.

## MATERIALS AND METHODS

This was a prospective case control study with 310 cases of intravitreal Bevacizumab injection given postinjection antibiotics while 310 cases of intravitreal injection given no antibiotics as control group. The later suggests that this

wasn't a consecutive series study. The patients were sorted out from OPD with the indications being exudative age related macular degeneration, macular edema due to CRVO, BRVO, Diabetes, Uveitis, proliferative retinopathies and choroidal neovascular membrane secondary to myopic degeneration. The study was carried out simultaneously at peoples University of Medical and Health Sciences Hospital Nawabshah and Ghulam Muhammad Medical College Sukkur between December 2013 and December 2014. The age of patients ranged between 30 to 70 years. All the injections were given in operation theatre with drape administered on the effected eye, washed with povidone iodine. The surgeon with aseptic measures after identifying the site of injection with caliper, 3.5mm in pseudophakic and 4 mm in aphakic eyes, either inferotemporal or superotemporal to limbus gave 0.05 cc of 1.25 mg Bevacizumab. Postinjection 310 patients were given tab Ciprofloxacin 500 mg per oral BD for 3 days along with topical Ofloxacin. On the other hand 310 were not given any medication. Patients with uncontrolled Diabetes and Hypertension were excluded from study. Those patients with any other intraocular surgical procedure performed at least 4 weeks before injection were also excluded.

All the Bevacizumab injections were brought from AKUH hospital with cold storage and were injected within 24 hours of arrival. Acute postoperative endophthalmitis was defined as the presence of progressive inflammation in the vitreous cavity and or anterior chamber within 4 weeks following intravitreal injection of bevacizumab. Postinjection patients were followed at 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> week. Immediate follow-up on 1st postinjection day was impractical as most patients of study belonged to remote areas and refused to follow back on 1st postinjection day. Keeping in view the ground facts the patients were called on 1st postinjection day to ask about any complain.

## RESULTS

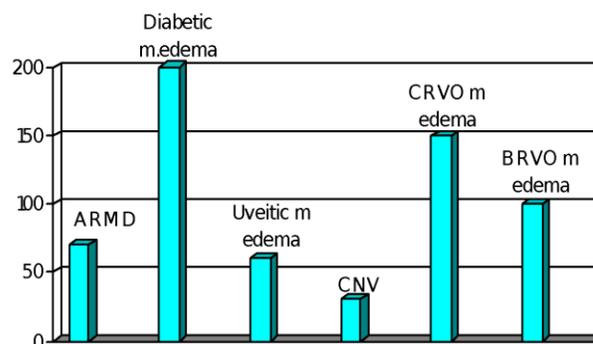
A total of 620 intravitreal injections of bevacizumab were performed for 480 eyes with macular edema due to diabetic retinopathy, CRVO and BRVO, uveitis as well as CNV and ARMD. Out of 620 injections 198 (31.93%) were reinjections. Follow up after each injection was at least 4 weeks. Case group with post injection oral ciprofloxacin 500mg and topical moxifloxacin were not different in any follow up than control group without any post injection antibiotic. No sign and symptom of acute postoperative endophthalmitis seen in any case. 5 (0.80%) patients showed fresh vitreous hemorrhage. No other complication seen.

## DISCUSSION

Endophthalmitis is a serious vision threatening ocular condition that can occur after intravitreal injections from exogenous approach.<sup>5</sup>

Bevacizumab is a recombinant humanized mono-clonal IgG1 antibody that inhibits human VEGF<sup>4</sup>. The intravitreal use of Bevacizumab for VEGF mediated disease such as choroidal neovascularization,<sup>6</sup> Central retinal vein occlusion, Proliferative diabetic retinopathy; pseudophakic cystoid macular edema<sup>11</sup> is well established. Though there has still not being long term studies in human, limited human and animal studies show that intravitreal Bevacizumab is safe.<sup>12,13</sup>

The risk factors for endophthalmitis in intravitreal injections are Diabetes, old age and Blepharitis. Insulin dependant diabetes and old age are risk factors for infection due to immunosuppression.<sup>14,15</sup> A general concept proved by studies is that most infections arouse from own flora<sup>16</sup>. This concept is further supported by the fact that blepharitis<sup>17</sup> is one of the major risk factor for postinjection endophthalmitis. Jonaset et al,<sup>18</sup> reported that the rate of infectious endophthalmitis after intravitreal injection of 1.5 mg Bevacizumab was 1:1000. Other studies reporting incidence of endophthalmitis after intravitreal injections of anti VEGF drugs include VISION clinical trial for Pegaptanib injection where infective endophthalmitis rate was 0.16%.<sup>19</sup> Another study by Macugen<sup>20</sup> used Pegaptanib in the treatment of diabetic macular edema found the endophthalmitis occurrence rate to be 0.15%. Ranibizumab a newer anti VEGF drug, with target on all active isoforms of VEGF - A showed endophthalmitis rate of 0.25% per injection in a study.<sup>21</sup> In the MARINA study the incidence of endophthalmitis was 0.05% per injection<sup>7</sup>. In a recent internet based survey Fung AE, et al, found the infectious endophthalmitis rate after intravitreal Bevacizumab to be 0.01%.<sup>4</sup>



**Fig. 1:** Number of patients according to indications.

Along with an established OT set up with all sterilization, disinfection of lid and conjunctiva with povidone iodine it is necessary to keep the needle of injection away from eyelashes which serve as nidus of infection. Although definite evidence does not exist to show that pre-injection and post-injection topical antibiotics drops reduce the incidence of endophthalmitis, enhanced topical

antibiotic concentration can facilitate antibiotic bioavailability in ocular tissue (aqueous humour, vitreous humour) and improve antibacterial efficacy. In this regard a recent study showed that although bacterial colony counts can be reduced by the use of topical antibiotic drops administered several days prior to procedure, topical antibiotic drops did not appear to reduce colony counts significantly more than topical povidone as a part of preparation alone.<sup>22</sup> In our study also no difference was found among the two groups who received post injection antibiotics and who do not received any antibiotic.

Many studies involving intravitreal injections without topical antibiotics have demonstrated a low risk of endophthalmitis.<sup>23-25</sup> Yet proved by Meredith TA et al.<sup>26</sup> Incidence of endophthalmitis was 0.15% among injections with no antibiotic use, 0.08% among injections with preinjection antibiotics only, 0.06% among injections with postinjection antibiotics only, and 0.04% among injections with preinjection and postinjection antibiotics. Recent large series have estimated this risk to be about one in 3,000 injections or less.<sup>27</sup> Another study with differing results showed that a low incidence of endophthalmitis can be achieved when topical antibiotics are omitted.<sup>28</sup> Park Y et al in his study concluded that the rate of endophthalmitis after intravitreal injection using aseptic techniques in the clinical practice setting is similar with or without the use of preinjection antibiotics.<sup>29</sup> However because of very low incidence of endophthalmitis no study can rule out the possibility that topical antibiotics might have some role in its incidence.

## CONCLUSION

The results of our study do not prove that topical antibiotics have no effect on reducing the risk of endophthalmitis following intravitreal injection. Further if strict preparation protocols of intravitreal Bevacizumab injection are followed including use of drape, topical povidone iodine and sterile speculum, the necessity of using postinjection antibiotics is minimal.

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