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Original article:

COMPARITIVE EFFICACY OF TWO ANTI VEGF DRUGS IN TREATING MACULAR PATHOLOGY RESULTING FROM VARIOUS RETINAL & CHOROIDAL VASCULAR DISORDERS

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ABSTRACT

Introduction: Diabetic Macular Edema, Macular Edema resulting from CRVO, BRVO and fluid collection in macula as result of exudative AMD are very common disorder we come across in our OPD. With the advancement of technological innovation earlier detection of these disorder are now possible and progress of treatment will be effectively titrated

Objectives: Objectives of the study is to evaluate the visual improvement with treatment of various intravitreal anti VEGF drugs which are given to the patients suffering from visual detoriation due to development of macular pathology by various retinal and choroidal vascular disorders.

Methods: This retrospective observational study was carried out from period of March 2017 to March 2018 in ophthalmic department of tertiary care eye hospital. Approval for this study was obtained from the institutional ethical committee of B.J. Medical College and Sassoon General Hospital, Pune.

Total number 36 Patients 40 eyes with age group from 43yrs-75 yrs., having diagnosis –Diabetic macular edema, wet AMD (exudative age related macular degeneration), CRVO, BRVO were included. They were treated with intravitreal anti VEGF injections e.g. Bevacizumab or Ranibizumab. Visual outcome was determined on the basis of best corrected visual acuity with Snellen's chart and macular thickness measurement was done with the help of Optical Coherence Tomography (SD-OCT) scan of eye.

Results: Visual improvement was significantly higher in wet AMD (exudative age related macular degeneration) , vascular occlusion, CRVO & In diabetic macular edema with intravitreal anti VEGF Bevacizumab and Ranibizumab injection.

Conclusion: Visual improvement was significantly higher with treatment of anti VEGF drugs in cases of macular pathology resulting from these retinal & choroidal vascular disorders.

Key words : DME (Diabetic Macular edema), wet AMD (exudative age related macular degeneration), CRVO (Central Retinal Vein Occlusion) , BRVO (Branch retinal vein occlusion), Anti VEGF (Vascular Endothelial Growth Factor), OCT (Optical Coherence Tomography)

Introduction:

Macular edema occurs when there is abnormal leakage and accumulation of fluid in the macular area from damaged blood vessels in the nearby retina. This leakage causes the macula to swell and leads to diminution of vision. Intravitreal injection of anti VEGF is effective in reducing macular edema.

Age related Macular degeneration (AMD) is the leading cause of irreversible blindness among elderly patients. [10, 11] Neovascular AMD is characterized by choroidal neovascularization [12] (CNV). Growth of abnormal vessels in the macular region, with subsequent fluid leakage results in sudden loss of vision [15]

Retinal vein occlusion (RVO) is the most common cause of retinal vascular disease after diabetic retinopathy. RVO causes unilateral and painless loss of vision. [1-3] they are diagnosed as CRVO or BRVO based on localization of occlusion located in central retinal vein. [4-5]

Treatment options for managing Macular Edema with RVO and DME, anti VEGF has now become the treatment of choice. [17]

Materials and methods:

Study design: This was a retrospective observational study.

Study site: Study was conducted in department of ophthalmology BJGMC and Sassoon General Hospital Pune.

Study Period: One year from March 2017 to March 2018.

Study Object: Total of 40 eyes of 36 patients in the age group of 43yrs-75 yrs were included in this study. They were divided into two groups, eyes that received intravitreal inj Ranibizumab for the treatment of macular edema (n= 17) and those received Bevacizumab (n=23)

Patients satisfying the inclusive criteria were enrolled in the study.

Inclusion criteria:

1. Patients with clinical diagnosis of DME, wet AMD, CRVO, BRVO
2. Foveal center involving macular edema
3. CST > 250 micro meter on SD-OCT
4. BCVA between 1/60 to 6/24
5. Controlled blood sugar (F- 100 mg, PP-180 mg) with or without anti hyperglycemic medication
6. Controlled BP (120/80 mmHg) with or without anti-hypertensive medication.

Exclusive criteria:

1. Administration of any other intravitreal drug during study period
2. Prior anti VEGF treatment of intra ocular corticosteroid use in the study eye
3. Pan- retinal laser photocoagulation or macular laser photocoagulation in the study eye.
4. History of intraocular surgery in the study eye
5. Patients having dense cataract where OCT assessment was not possible
6. Patients not willing for enrollment

Study Procedure:

Written informed consent was obtained from all the patients enrolled in the study before treatment. All the patients received complete ocular examination including BCVA testing, CST measurement by SD-OCT, dilated fundus examination with indirect ophthalmoscope, slit lamp, bio microscopy with +78D and +90D, color fundus photography and fluorescein angiography at baseline. BCVA was measured with standard Snellen chart at 6 meters.

All the patients were treated with intravitreal inj. Ranibizumab (0.5mg/0.05ml) and inj. Bevacizumab (1.25mg /0.1ml). Three injections at 4 weeks intervals were given to each patient. Patients were followed up for period of 6 months.

Intravitreal injection:

Intravitreal Ranibizumab (0.5mg/0.05ml) and Bevacizumab (1.25mg/0.1ml) injections were prepared in the operative room under sterile conditions. Topical 5% povidone iodine eye drops and topical anesthetic eye drops were applied in the study eye and lid speculum was inserted after painting and draping done with 10% povidone iodine solution. Intravitreal inj (0.5mg/ 0.05ml) Ranibizumab and intravitreal inj (1.25mg/0.01 ml) Bevacizumab was injected via pars plana route with 30 gouge needle at a distance from limbus 4mm in phakic eye, 3.5mm in pseudo phakic and 3 mm in aphakic patient. The needle was carefully removed using a sterile cotton applicator to prevent reflux. Indirect ophthalmoscopy and tonometry were performed after the procedure to detect any injection related complications. After injection an antibiotic eyedrops were applied every 6 hrs for 1 week.

Follow-up Examination:

The primary outcome included mean change from baseline BCVA, the mean change from baseline of CST as assessed by SD-OCT. Follow up examination was performed every month for 3 initial intravitreal injections. BCVA, fundus examination, tonometry and CST measurement with SD- OCT were assessed at each follow up visits. The secondary outcome was incidence of ocular adverse events.

Adverse Events:

Ocular adverse events included the increased intraocular pressure in 4 patients (three eyes in Bevacizumab group and one eye in Ranibizumab group). That was controlled with topical medication. There was no significant difference in adverse events between the Ranibizumab and Bevacizumab groups. None of the patients in the study developed endophthalmitis, retinal detachment, retinal tears, injection related cataract or vitreous hemorrhage.

Statistical Analysis:

Two tailed paired students t-tests were performed to analyze visual outcomes. A Bonferroni correction was used to account for multiple comparisons using = 0.05, the adjusted P value was determined to be 0.007.

Results:

The study conducted 40 eyes of 36 patients, 30 men (83.33%) and 6 women (16.67%). The patients ages ranged from 43yrs to 75 yrs., with mean age of 59±6 (mean ± standard deviation) (SD) Out of 40 eyes 17 eyes received intravitreal inj. Ranibizumab and 23 eyes received intravitreal inj. Bevacizumab. The mean visual acuities at baseline were 6/60 in the ranibizumab and bevacizumab groups. The mean CST value at baseline were 480±150 micrometer in both groups

Visual acuity and CST outcome:

At 6 month the mean BCVA significantly improved by 4.5 letter in bevacizumab and ranibizumab groups ($P<0.001$). There was no significant difference in the change in BCVA between ranibizumab and bevacizumab groups.

The reduction in CST at 6 months was 250 to 150 micrometers ($P<0.001$). There was no significant difference between ranibizumab and bevacizumab group in the reduction of the CST.

The mean number of inj. administered during the 6 months treatment period was three in both bevacizumab and ranibizumab.

Discussion:

=Improved visual acuity and reduction in macular thickness was observed in patients with macular edema associated with wet AMD, DME, RVO but elevated intraocular pressure observed in the treatment of both groups. [13, 14] Yilmaz and Cordero-Coma[2] and Ehlers et al[3] showed that Bevacizumab brought about significant improvement in visual acuity and reduction in CST in patients with RVO. Randomized controlled trials have demonstrated the efficacy and safety of intra vitreal Ranibizumab and Bevacizumab for stabilizing and improving visual acuity in wet AMD. [15, 16]

The trial assessed the efficacy of Ranibizumab in patients with RVO and found a significant improvement in visual acuity and reduction in central sub foveal thickness in Ranibizumab group compared to Sham group.[1]

Anti VEGF levels are increased in vitreous cavity and retina in diabetic retinopathy. VEGF increases the retinal vessels permeability, leads to perivascular leakage and macular edema. Anti VEGF agents Ranibizumab and Bevacizumab are equally effective for reducing macular edema and improves visual acuity in DME. [18]

Both Ranibizumab and Bevacizumab are humanized monoclonal anti VEGF anti bodies. Ranibizumab consist of 49 kD Fab fragment and Bevacizumab consist of 149 kD full length anti body.[4, 5] Ranibizumab have a greater ability to penetrate than Bevacizumab because of its molecular size. [6, 7] Ranibizumab is also known to more potently neutralize anti VEGF than bevacizumab does in vitro. In our study both agents have shown equivalent effect on treatment wet AMD and RVO [8, 9]

Limitations:

There are some limitations of this study relatively short follow up time and availability of less number of injections of Ranibizumab, as cost is much higher than Bevacizumab. Also we could not give more than 3 injections to each patient.

Conclusion:

In this retrospective observational study on wet AMD, DME and RVO both Ranibizumab and Bevacizumab are effective for treatment of macular edema. Visual improvement was significantly higher with treatment of anti VEGF drugs in cases of macular pathology resulting from these retinal and choroidal vascular disorders. These anti VEGF's are also effective in reducing macular thickness and improving visual acuity.

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