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COMPARISON OF VISUAL ACUITY OUTCOME IN PROLIFERATIVE DIABETIC RETINOPATHY(PDR) BETWEEN INTRAVITREAL BEVACIZUMAB AND RANIBIZUMAB INJECTIONS

Ophthalmology

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ABSTRACT

PURPOSE: Diabetic Retinopathy is one of the worst complications of diabetes and can threaten sight. The aim of this study is to compare the visual acuity outcome in proliferative diabetic retinopathy(PDR) with clinically detectable macular oedema after intravitreal administration of either bevacizumab or ranibizumab.

METHOD: Data were analysed retrospectively in which 80 eyes of 64 patients were enrolled. They were divided into two groups by simple random sampling, 40 PDR eyes treated with bevacizumab in group A and 40 PDR eyes treated with ranibizumab in group B. Visual acuities along with basic demographic characteristics were noted down. The changes in best corrected vision(BCVA) and the number of injections required were compared between the two groups. **RESULTS:** The study included 80 eyes of 64 patients, out of which 52 were phakic and 28 were pseudophakic. At the end of 1 year, in Group A 10 eyes(25%) showed no changes in visual acuity, 29 eyes(72.5%) showed improvement between LogMAR 1.00 to 0.48 and 1(2.5%) showed visual acuity less than LogMAR 0.33. In Group B, 8 eyes(20%) showed no changes, 30 eyes(75%) showed improvement between LogMAR 1.00 to 0.48, 2 eye(5%) showed visual acuity less than LogMAR 0.33 Group A and Group B showed similar efficacy after same number of intravitreal injections administered and similar follow-up.**CONCLUSION:** Our results show that ranibizumab and bevacizumab are more or less similar in terms of visual acuity outcome. At the same time bevacizumab is more cost-effective than ranibizumab. Further trials needs to be done using bevacizumab. The success of anti-VEGF treatment depends not only on the treatment of active disease, but also on the prevention of disease of disease worsening. Planning the next anti-VEGF injection treatment helps to minimize the possibility of delays in treatment. The present covid-19 lockdown restrictions has affected in the treatment causing delay.

KEYWORDS

proliferative diabetic retinopathy, bevacizumab, ranibizumab, visual acuity.

INTRODUCTION :

Angiogenesis is defined as the formation of new blood vessel from the existing vasculature. Complex interactions are involved between non vascular and microvascular cells. Among the growth factors, vascular endothelial growth factor(VEGF) has emerged as the most important causal agent of angiogenesis in health and disease of the eye.[1]

Many ocular diseases are characterized by angiogenesis, including diabetic retinopathy, age- related macular degeneration, retinopathy of prematurity[2]. In all these conditions, angiogenesis is probably stimulated by local hypoxia resulting from neuronal metabolism. Hypoxia is implicated in loss of retinal ganglion cells(RGCs) which occurs by apoptosis or necrosis. Hypoxia- ischemia induces the expression of hypoxia inducible factor-1alpha and its target genes such as vascular endothelial growth factor(VEGF) and nitric oxide synthase(NOS). Increased production of VEGF causes disruption of blood retinal barrier leading to retinal edema.[3]

With recent advancements it is possible to modulate vascular endothelial growth factor and its receptor (VEGF-VEGFR system). Drugs such as bevacizumab, ranibizumab, aflibercept and pegaptanib have proven effectiveness in treatment of several ocular diseases such as age-related macular degeneration, macular oedema, proliferative retinopathies and iris neovascularization.[4,5]

The indications for the application of anti-VEGF therapy in ophthalmology are becoming wider and wider. It may also be used in anti-glaucoma procedures[6] and corneal pathologies.[7]

Proliferative Diabetic Retinopathy(PDR) is the leading cause of blindness.[8] It is characterized by growth of neovascular vessels, which are prone to leakage, bleeding, development of vitreoretinal membranes as well as tractional retinal detachment and neovascular glaucoma. Risk of vision loss is significantly higher in PDR than NPDR and PDR is more prevalent in Type 1 diabetes and younger age groups.[9] The Diabetic Retinopathy Study(DRS) found that almost half of the eyes with PDR and high risk characteristics will progress to severe vision loss(Va less than 5/200) without treatment.[10]

Bevacizumab(Avastin;Genecteh,SanFrancisco,CA,USA) is a full length recombinant humanized anti-VEGF monoclonal antibody, approved by the US Food and Drug administration for the treatment of colorectal cancer.[11] It is a large sized molecule(molecular weight-148kDa) and has twice half-life than ranibizumab.[12]

Ranibizumab(lucentis;GenetechUSA,Inc,CA,USA) is an engineered, humanized, recombinant antibody fragment(Fab) active against all VEGF-A isoforms. It lacks the Fc domain and has a shorter half-life than other anti-VEGF agents.[13] Lucentis is presently licensed(FDA Approved) as an intravitreal agent for the treatment of wet age-related macular degeneration(AMD)

METHOD :

In this prospective, comparative, interventional study, we reviewed the records of the Proliferative Diabetic Retinopathy(PDR) patients with clinically detectable macular edema who had a baseline visual acuity 1.0LogMAR (Snellen's chart value 6/60) and treated with intravitreal Bevacizumab and Ranibizumab on and as needed treatment between 1st October 2020 and 31st September 2021 over a period of 1 year. A written informed consent was obtained from all patients and the study adhered to the tenets of the Declaration of Helsinki . Approval was taken from Institutional Ethical Committee. The inclusion criteria were : Age >45 years , BCVA LogMAR 1.0, minimum follow up of 6 months. Patients were not included in the study if they had any Vitreous Haemorrhage, Tractional Retinal Detachment, Fibrovascular Proliferation or any other retinal disease disease or photodynamic therapy was already given, or if they were treated with other retreatment regimens or if all follow up data were not available. The patients who received other drugs intravitreally like steroids and antibiotics were excluded. The included patients underwent a standardized examination including measurement of BCVA(visual acuity was measured using Snellen chart then converted to LogMAR for statistical analyses), slit-lamp biomicroscopy, intraocular pressure(IOP) measurement using applanation tonometry and fundus examination, DFA was done to diagnose PDR.We divided the patients into two groups. Group A comprised of patients who had received intravitreal bevacizumab injection and Group B comprised of patients who had received intravitreal ranibizumab. The dose of both were taken as 0.05ml under sterile conditions after topical anaesthesia,10%

povidone iodine was used on the lids and lashes and 5% povidone iodine was administered on the conjunctival sac. Intravireal bevacizumab or ranibizumab was injected through the pars plana at 4mm or 3.5mm in phakic or pseudophakic eyes respectively posterior to the limbus with a 30 guage needle. Patients were instructed to return to the hospital if they experienced eye pain,decreased vision or any other symptoms. Primary outcome measure was the change in BCVA from baseline to 1 year. Secondary outcome was the number of injections received within 1 year.

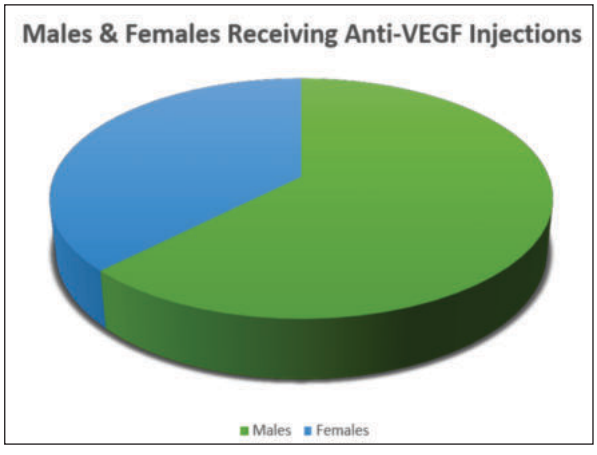
Statistical Analysis:

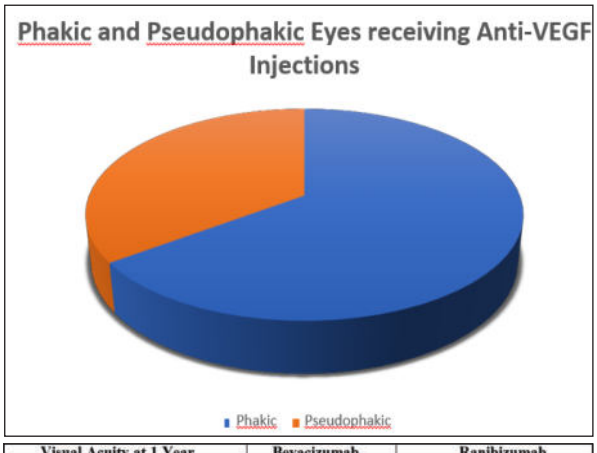
Visual acuity was converted to the logarithm of the minimum angle of resolution(LogMAR) for statistical analysis. Categorical variables were presented as numbers and percentages, while numerical variables were expressed as the mean and standard deviation. The baseline characteristics and outcome measures between the groups were compared variables . Kolmogorove-Srirnov test were used to analyse the distribution of the samples , and chi-square test and Fisher exact test were performed to compare catagoric data. The statistical evaluation was performed using SPSS(version 17.0). A p value of less than 0.05 was considered to be statistically significant.

RESULTS:

The total number of eyes were 80 of 64 patients. Out of 64, 40 (62.5%) patients were males and 24 (37.5%)patients were females. 48(60%)eyes received the anti-VEGF injections in right eye and 32(40%) in left eye. 52 (65%) eyes were phakic and 28(35%)eyes were pseudophakic.

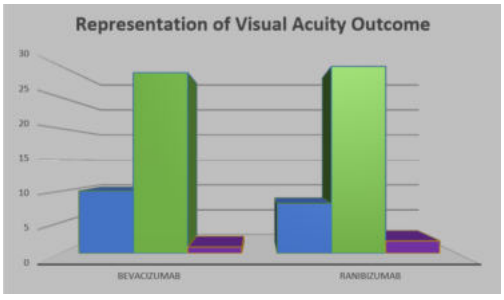
At the end of 1 year, in Group A 10 eyes(25%) showed no changes in visual acuity, 29 eyes(72.5%) showed improvement between LogMAR 1.00 to 0.48 and 1(2.5%) showed visual acuity less than LogMAR 0.33. In Group B, 8 eyes(20%) showed no changes, 30 eyes(75%) showed improvement between LogMAR 1.00 to 0.48, 2 eye(5%) showed visual acuity less than LogMAR 0.33.





Visual Acuity at 1 Year	Bevacizumab	Ranibizumab
Unchanged	10(9.00) [0.11]	8(9.00) [0.11]
VA 1.0-0.48	29(29.50) [0.01]	30(29.50) [0.01]
VA < 0.3	1(1.50) [0.17]	2(1.50) [0.17]
Total	40	40

The chi-square statistics is 0.5725. The p-value is 0.751073 (>0.5, not significant)



DISCUSSIONS:

The anti-VEGF medications are an important aspect in the treatment of PDR. The Protocol T comparison of bevacizumab, ranibizumab, aflibercept showed that diabetic retinopathy regression was observed using the anti-VEGF (14)

Anti-VEGF can be used as an adjunct to PRP or solely. Protocol S demonstrated that ranibizumab alone was noninferior to PRP (15). Some studies have shown similar results like ours (16). In view of cost bevacizumab can be used as an alternative to ranibizumab as its cheaper and easily available with similar effectiveness(17) These studies suggest that anti-VEGF can be started in early or severe NPDR or PDR disease course and aggressive treatment may be necessary in severe PDR.

Major ocular adverse effects of anti-VEGF intravitreal injections, such as intraocular pressure rise, are transient but may be relevant in glaucoma patients. Serious adverse effects like endophthalmitis are rare but accumulate with continuous injections. In PDR there is also risk of tractional retinal detachment after anti-VEGF use in eyes with pre-existing vitreoretinal membranes, which can lead to vision loss.

CONCLUSION:

In conclusion, the results of this study implies that the best corrected visual acuity (BCVA) is similar using intravitreal ranibizumab and bevacizumab in Proliferative Diabetic Retinopathy (PDR) with clinically detectable macular oedema after 3 injections of anti- VEGF (4weeks interval). Bevacizumab injections are cost-effective and easily available than Ranibizumab.

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