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EFFICACY OF RANIBIZUMAB IN CHRONIC CENTRAL SEROUS CHORIORETINOPATHY ASSOCIATED WITH RETINAL PIGMENT EPITHELIAL DETACHMENT: A RETROSPECTIVE STUDY.

Ophthalmology

Bivas Bala*

Assistant Professor, Department Of Ophthalmology, Malda Medical College, West Bengal, India. *Corresponding Author

ABSTRACT

AIM: To evaluate the efficacy of intravitreal ranibizumab in chronic central serous chorioretinopathy associated with retinal pigment epithelial detachment.

METHODS: In this retrospective study a total of 21 patients diagnosed with chronic central serous chorioretinopathy with pigment epithelial detachment were treated with intravitreal ranibizumab from Jan 2017 to Nov 2019 at Malda medical college, West Bengal, India. From the history sheet we were noted each patient's best spectacle corrected visual acuity. Measurement of central macular thickness and subfoveal choroidal thickness were recorded from OCT report. After getting informed consent all patient received intravitreal ranibizumab injection at monthly interval until central macular thickness reduced to normal. Patient were followed up monthly interval for at least 6 months by measuring best corrected visual acuity and central macular thickness as well as subfoveal choroidal thickness. We were taken these data specially of 3 and 6 months for analysis. This data was analyzed statically by pair T test to determine the effectiveness of intravitreal ranibizumab in this condition.

RESULTS: all patients showed statically significant improvement within 3 months in terms of best corrected visual acuity, central macular thickness as well as choroidal thickness (p=<0.001) and these were well maintained at 6 months.

CONCLUSION: Intravitreal ranibizumab is a good therapeutic option in patients of chronic central retinopathy when it also associated with retinal pigment epithelial detachment.

KEYWORDS

Chronic central serous chorioretinopathy, pigment epithelial detachment, ranibizumab, choroidal neovascular membrane.

INTRODUCTION

Central serous chorioretinopathy (CSC) is a common macular disorder characterized by serous retinal detachment sometimes associated with retinal pigment epithelial (RPE) detachment, with leakage of fluid through the RPE into the subretinal space. Originally described by von Graefe (1) in 1866, Maumenee (2) first described fluorescein angiographic (FA) characteristics; fluorescein leakage at the level of the RPE revealed that the choroid and RPE were the primary tissues involved here. Gass then studied the angiographic findings and coined the term central serous chorioretinopathy (3).

Mudvari et al. (4) suggest that around 10% cases of central serous chorioretinopathy also have retinal pigment epithelial detachment. Latter Zhang et al. by doing spectral domain OCT showed a much higher percentage of pigment epithelial detachment both in acute as well as chronic CSCR (5). according to OCT features PED classified into two category flat irregular PED and focal PED. Flat irregular PED which is more commonly associated a poor prognosis, because they are more commonly associated with choroidal neovascularization. A recent meta-analysis by shangli et al (6) showed good outcome after intra-vitreal Bevacizumab on chronic CSCR when it was associated with flat irregular pigment epithelial detachment.

Ranibizumab a monoclonal anti VGEF with greater penetration than Bevacizumab already showed promising result for resolution neurosensory detachment in acute CSR as suggested by Kim et al in their study (7).

In this retrospective study we assess the efficacy of intravitreal ranibizumab in chronic central serous chorioretinopathy when it associated with retinal pigment epithelial detachment.

METHODS

This hospital based nonrandomized retrospective interventional clinical study was done at Malda Medical College, West Bengal, India from Jan 2017 to Nov 2019. We have evaluated the treatment sheet of all patients who were diagnosed as chronic central serous chorioretinopathy with retina pigment epithelial detachment during this period.

We recorded baseline feature of all patients including best-corrected visual acuity, Fundus fluorescein angiography, SD-OCT of macula and OCT angiography of the affected eye. Nature of previous treatment also noted. Now those patients who receive intravitreal ranibizumab after getting informed consent were included in this study. All those patients who receive ranibizumab previously or those who had others ocular disease were excluded from this study. All injections were given by a single surgeon following standard protocol. No intra or postoperative complications were noted during this period. Intravitreal injection was repeated at monthly interval until central macular thickness is reduced to 250 µm or less or patient's gets at least 3 consecutive injections in 3 months. Patient were followed up monthly interval for at least 6 months by measuring best corrected visual acuity and central macular thickness as well as subfoveal choroidal thickness. In each month visit SS-OCT was done to determine the measurement of central macular thickness and subfoveal choroidal thickness. All patients were followed up for at least 6 months. We were taken these data especially data of 3 and 6 months for statistical analysis. This data was analyzed statically by pair T test (www.select-statistics.co.uk) to determine the effectiveness of intravitreal ranibizumab in this condition in terms of best corrected visual acuity, central macular thickness and subfoveal choroidal thickness.

RESULTS

During study period there was total 33 patients with history of chronic CSCR with PED attended to our out patients department clinic. Of them 12 patients were excluded from this study as they have previously received intravitreal ranibizumab or they had ranibizumab related contraindication.

Of these 21 patients 16 were male and remaining 5 patients were female. The mean age of patients was 34.2 years (SD 9.32). The mean best corrected visual acuity before giving ranibizumab was 0.66 on logMAR unit (SD=0.19). Visual acuity was improved significantly after 3 months with a mean value of 0.3 logMAR unit (SD=0.139) and it is statically significant (p=<0.001%). This vision was well maintained even at 6 months. (Mean value 0.3 logMAR unit, SD=0.139).

Table 1: Baseline character of patients

No. of Patients	21
Male	16
Female	05
Mean Duration of symptom	7.4 months (Range: 12-4 months. SD: 2.13)
Mean visual acuity (logMAR).	0.6 (Range: 0.3-1.0. SD: 0.19)
Mean subfoveal choroidal thickness	521.7 µm (Range: 463-593. SD: 40.06)
Mean central macular thickness	426.8 µm (Range: 353-473. SD: 33.93)

The mean central macular thickness before injection was 426.8 micron (SD=33.93) and decreased to 241.5 µm (SD=23.07, p=<0.001%) at 3 months which was well maintained at 6 months interval (245.8 micron (SD=21.40 and P=<0.001%). The mean subfoveal choroidal thickness before injection was 521.7 micron (SD=40.06) and decreased to 374

µm (SD=31.08, p=<0.001%) at 3 months which was well maintained at 6 months interval (381 microns (SD=28.40 and P=<0.001%). The mean number of intravitreal ranibizumab injection was 2.8 (SD=0.91).

Table 2: Outcome measures at 3 and 6 months

Mean visual acuity (logMAR).	**at 3 months**	**at 6 months**
Mean central macular thickness	0.3(P<0.001%)	0.3(P<0.001%)
Mean subfoveal choroidal thickness	241.5µm (P<0.001%) 374 µm (P<0.001%)	245.8 µm (P<0.001%) 381 µm (P<0.001%)

DISCUSSION

Central serous chorioretinopathy usually a benign self-limiting condition where idiopathic detachment of neurosensory retina may occur because of the leakage from choriocapillaries via retinal pigment epithelium.

According to Spitznas hypothesis (8) abnormal ion transport across the retinal pigment epithelium and focal choroidal vasculopathy is main culprit behind central serous chorioretinopathy.

Indocyanine green angiography show choroidal ischaemia, choroidal vascular congestion and vascular hyperpermeability at multiple site during an attack of CSCR. This condition often associated with Retinal pigment epithelium damage because of the shedding of outer photoreceptor segment with intact blood retinal barrier, which result in accumulation of fluid in sub retinal space.

In chronic CSCR about one-third patients showed neovascularization at choroid suggesting neovascular may be reason behind such chronicity.

As it is a self-limiting benign condition most of the cases does not require any treatment, observation alone is sufficient but it needed longer time to resolve and associated with high recurrence rate. Studies suggest numerous options for the treatment of CSCR including observation, photodynamic therapy, focal laser photocoagulation, micropulse diode laser, ACE inhibitor.

Laser photocoagulation has a faster resolution of SRF absorption but may lead to scotoma in central visual field because of RPE damage. Photodynamic therapy causes choroidal hypoperfusion to resolve CSCR but associated with high cost and limited availability in India.

In recent studies it is found the CSCR with PED has strongly associated with choroidal hyperpermeability and neovascularization hence treating these patients with anti VGEF has logic.

A study by chen et al. (9) showed at least one-line improvement of visual acuity after receiving monthly bevacizumab injection for 3 consecutive months with fluorescein angiography showed absence of leakage with decrease central macular thickness. Schaal et al. (10) treated 12 eyes with bevacizumab injection (1-3 injection). After 6 months of follow up mean BCVA increased by 2 lines(P<0.02).

Ranibizumab is a recombinant humanized IgG1 monoclonal antibody fragment that binds to and inhibit vascular endothelial growth factor A (11). With smaller molecular weight, it penetrates better than bevacizumab and possibly better to counteract choroidal vascular permeability in CSCR with PED.

Kim et al. (7) already reported effectiveness of intravitreal ranibizumab in acute CSCR (less than 3 month). After single intravitreal injection it causes faster resolution of neurosensory detachment.

Another study at Turkey by Tekin K, Sekeroglu MA et al. (12) suggested that both ranibizumab and bevacizumab were effective in achieving rapid resolution of serous detachment in patients with acute CSC.

Our result demonstrated that one to three consecutive monthly intravitreal ranibizumab injection in chronic CSCR with retinal pigment epithelial detachment produce with faster visual recovery associated with reduction of central macular thickness as well as sub foveal choroidal thickness. No notable side effect was seen in any patients during this study.

CONCLUSION

Chronic central serous retinopathy when associated with pigment epithelial detachment often associated with a poor visual outcome. A wide range of treatment options likes photodynamic therapy, focal laser photocoagulation, micropulse diode laser, ACE inhibitor are available for chronic central serous chorioretinopathy but none are proven beneficial when this condition associated with pigment epithelial detachment. Bevacizumab may prove beneficial but has serious vision threatening complication.

We found intravitreal ranibizumab produce a speedy recovery in term of central vision improvement as well as improvement of central macular thickness and sub foveal choroidal thickness in patients with chronic CSCR with PED. As it is a small single centre retrospective study, a larger prospective multi-centre study is needed in this regard.

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