EFFECT OF INTRAVITREAL BEVACIZUMAB FOR ACUTE CENTRAL SEROUS CHORIORETINOPATHY

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ABSTRACT

Purpose: Background objective of this clinical trial is to evaluate the anatomical and functional outcomes of intravitrealbevacizumab (IVB) in acute central serous chorioretinopathy (CSCR).

Materials and Methods: The study was conducted at khattak eye center from February 2018 to july 2018. In a randomized clinical trial 16 CSCR eyes (with <1-month disease history) were examined by the end of the one, three and six month. Initially, all the patients were examined for the best corrected visual acuity (BSCVA) underwent anterior and posterior segment examinations. Then, fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) was performed to confirm the diagnosis. The patients were divided in to two groups each of 8 subjects. Group-A bevacizumab (1.25 mg), group-B did not receive any treatment (control group).

Results: The mean age was 35.7years ± 7.2SD (ranged from 27 to 50 years). All the patients followed for 6 months periods.There was insignificant difference in the vision of two groups at 6 months (P = 0.727).There was no significant difference noted between the two groups, interventional and control group in the maximum central macular thickness at 6 month after injection (P = 0.922).

Conclusion: There was insignificant difference between IVB injection and observation in terms of visual outcomes, however central macular thickness decreased at one month in IVB group but no significant deference noted at 6 months.

Keywords: IntravitrealBevacizumab (Avastin), Central Serous Chorioretinopathy, Macular Thickness, Observation

INTRODUCTION

Central serous chorioretinopathy (CSC) is a condition of serous detachment of the neurosensory retina from retinal pigmented epithelium at the posterior pole due to active retinal pigment epithelial (RPE) leakage.[1,2] There was no significant difference between IVB injection and observation in terms of anatomical outcomes of treatment for CSCR. In terms of visual outcomes, observation was superior to IVB injection. Keywords: Intravitreal Bevacizumab (Avastin), Central Serous Chorioretinopathy, Macular Thickness, Observation

Gass postulated that leakage of fluid into the subretinal space is due to an increase in the permeability of choriocapillaries results in RPE detachment.[3] Enhanced depth imaging optical coherence tomography (EDI-OCT) also showed that the choroid is very thick in patients with CSCR which might indicate increased hydrostatic pressure in the choroid.[4,5] Usually in 90% of cases CSRC patients recover spontaneously so most of the clinician prefer to observe these patient in acute cases.[6] However, these modalities may entail complications including RPE changes, choriocapillarishypoperfusion and secondary choroidal neovascularization, or may not be sufficiently effective.[7,8,9,10] Conventional treatments such as laser photocoagulation or photodynamic therapy (PDT) which is rarely used now a days but still have been used in some cases with acute or chronic CSCR.[11]Vascular permeability is one of the essential step vascularization, Vascular endothelial growth factor (VEGF) which is blamed as major mediator of neovascularization is produced by retinal and choroidal cells in response to ischemia.[12]Antibodies to VEGF may reduce choroidalhyperpermeability. Bevacizumab (Avastin; Genentch Inc., San Francisco, CA, USA), a humanized monoclanal antibody to VEGF, it block the VEGF and prevent neovascularization. Recently, a number of reports have demonstrated favorable outcomes after intravitrealbevacizumab (IVB) injection without serious adverse effects in patients with CSCR.[13-16]

In this study, we aimed to compare the anatomic and functional outcomes of IVB injection in patients with CSCR and compare it to that in patients who did not receive any intervention and were simply observed.

MATERIALS AND METHODS

The study was conducted at khattak eye center from February 2018 to july 2018. In a randomized clinical trial, 16 CSC eyes (with <1-month disease history) were examined by the end of the one ,three and six month. In this study there was a special protocol for each patient, best corrected visual acuity (BCVA) in snellen units, applanationtonometery, fundus examination, fluorescin angiography and optical coherence tonometry (OCT)

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were recorded at base line.Certain baseline line investigations like central retinal characteristics were analyzed using OCT through a dilated pupil. Optical coherence tomography (OCT) was also used to confirm the diagnosis. The patients were divided in to two groups each of 8 subjects. Group-A bevacizumab (1.25 mg), group-B did not receive any treatment (control group). All those patients who had received any treatment for CSCR like photodynamic therapy or focal thermal laser photocoagulation or who had choroidal neovascularization, polypoidalchoriovasculopathy, or other maculopathy on clinical examination, fluorescein angiography, were excluded from the study. All subject were bound to sign the informed consent. Patients were randomly divided into the IVB group or the observation group at a ratio of 1:1. The patients were randomized using computerized randomization table.All those patients in the IVB group received only a single intravitreal injection of bevacizumab (1.25 mg in 0.05 mL) under standard protocol conditions. The observation group have no interventions and was observed without any any medication.

Regarding follow-up, the patients were examined at one month and three months with slit-lamp bio microscopy and OCT, and fluorescein angiography was performed as decided by the examiner. No other treatment for CSC was performed during the study. The main outcome of the study was the time from baseline to complete absorption of subretinal fluid during follow-up. Secondary outcome were OCT central macular thickness included serial changes in the visual acuity.

Statistical analyses were performed using a commercially available statistical software package (SPSS ver. 11.5; SPSS Inc., Chicago, IL, USA). Snellen units were used to converted in logMAR units for the purpode of statistical analysis.

RESULTS

Total of 22 eyes included in the whole periods of study. There was irregular followup with the 6 patients and 2 eye have with the lack of post-IVB OCT data so total of 8 eyes were excluded. Total of 16 eyes with 6 months of follow-up were ultimately included in this study. The mean age of the patients were 35.7 years ±7.20 SD in group A and 37.22 years ±8.20 SD in group B. Gender distributions were 12 men and 4 women. Both the groups have 8 patients (8 eyes). There was no ocular or systemic complications noted during the study periods after IVB. Demographic data on age, sex, laterality of the eyes and symptoms showed insignificantdeference between the 2 groups. There was no significant deference noted between the two groups in terms of baseline visual acuity (logMAR) and baseline CMT. The baseline data of the 2 groups are shown in table-1.

Both the groups had complete resolution of submacular fluids during the 6 months of periods.Mean baseline logMAR visual acuity was 0.41 ± 0.38 in the IVB group which improved to 0.10 ± 0.13 at final followup (P = 0.947); mean baseline logMAR visual acuity was 0.42 ± 0.36 in the observation group and improved to 0.12 ± 0.14 at final followup (P = 0.0.947). Although, Improvement was more observed in the IVB group as compared to the observation group but statistically it was insignificant. Similar findings were recorded when compared the difference in improvement in both the groups. Changes in logMARvisual acuity also give insignificant results with p-value=0.922 as shown in Table 2. None of the patients in either group lost vision during followup

The mean visual acuity of the 2 groups showed normal pattern and foundno difference at any visit during the follow-up period which can be clearly observed in Fig. 1

DISCUSSION

Acute central serous chorioretinaopathy is a duration of symptoms and/or retinal detachment which is less than 6 months and retinal pigment epithelium leakage on fluorescin angiography.[17,18]Currently there is no standard therapy for acute CSC, even though there have been many treatment modalities studied including laser photocoagulation, PDT, and pharmacological agents.[19,20] Treatment of acute CSC with intravitreal injections of anti-VEGF agents has variable outcomes.[21,22] Lim et al. demonstrated that VEGF and IL-8 levels were not elevated in the aqueous humor and plasma of CSC

Table 1: Baseline data of the acute central serous chorioretinopathy patients

Characteristics	Observation (n=8)	IntravitrealBevacizumab (n=8)	P-value
Age (years)	35.72+7.0	37.22+8.20	0.8568
Gender (M:F)	7:1	8:0	0.1517
Laterality (Right:Left)	3:5	6:2	0.1306
Duration of current CSC episodes(wk)	5.4+1.6	5.0+1.3	0.5924
Spherical equivalent refractive error (Diopter)	0.50+1.5	0.50+1.2	0.9999
Baseline central macular thickness (um)	460+120	420+102	0.4844

Table 2: Comparison of Visual Acuity In Both The Groups

	Group	N	Mean	Std. Deviation	p-value
Baseline Visual Acuity	IVB	8	.4125	.38336	0.947
	Observation	8	.4250	.36154	
Post Visual Acuity	IVB	8	.1000	.13093	0.727
	Observation	8	.1250	.14880	
Difference in Visual Acuity	IVB	8	.3125	.26959	0.922
	Observation	8	.3000	.23299	

patients compared with a healthy group.[23] In light of these findings, further investigations are required with regard to the mechanism and results of intravitreal anti-VEGF treatment in acute CSC.Bevacizumab is anti VEGF which is a full length antibody that binds all form of VEGF a lot of evidence available at literature which support the safty and efficacy of the drug in many disorders.[24,25]Although the direct role of the IVB in cases of acute CSC is not available.There is an evidence of choroidal lobar ischemia, venous congestion and multiple area of hyperpermeability in patient with acute CSC on indocyanine green angiography.[26,27]

There are two reports available about the IVB treatment in patients with CSC. Although reports about the level of VEGF in CSC patient are not available in the literature.Torres-Soriano et al.[28]treated 5 eyes of CSC with the use of IVBI and he found the procedure very safe and visual improvement noted in most of the cases. Seonget al.[29] also studied 10 eyes with IVBI and have a very promising results in resolution of the sub macular fluids with in one month. The study was without control group and small case series.

Our results shows that, in cases of acute CSC all the patients with IVBI treatment showed no satisfactory results in terms of earlier remission, functional or anatomical r There are several limitations to this study including the small number of patients and the retrospective nature of the study. Further prospective randomized controlled studies are necessary to determine the efficacy of anti-VEGF treatment in CSCR.

CONCLUSION

We found no significant differences between IVB injection and observation regarding anatomical outcomes of treatment in CSCR. In terms of functional outcomes, observation was even superior to IVB injection.

REFERENCES

1. Piccolino FC, Borgia L. Central serous chorioretinopathy and indocyanine green angiography. Retina. 1994;14(3):231–42.
2. Wang M, Munch IC, Hasler PW, Prünte C, Larsen M. Central serous chorioretinopathy.ActaOphthalmol. 2008 Mar;86(2):126–45.
3. Gass JD. Pathogenesis of disciform detachment of neuroepithelium: II. Idiopathic central serous choriodopathy. Am J Ophthalmol. 1967;63:587–615.
4. Prünte C, Flammer J. Choroidal capillary and venous congestion in central serous chorioretinopathy. Am J Ophthalmol. 1996 Jan;121(1):26–34.
5. Tittl MK, Spaide RF, Wong D, Pilotto E, Yannuzzi LA, Fisher YL, Freund B, Guyer DR, Slakter JS, Sorenson JA. Systemic findings associated with central serous chorioretinopathy. Am J Ophthalmol. 1999 Jul;128(1):63–8.
6. Chan WM, Lai TY, Lai RY, Liu DT, Lam DS. Half-dose verteporfin photodynamic therapy for acutecentral ser00ous chorioretinopathy: One-year results of a randomized controlled trial. Ophthalmol.2008;115:1756–65.
7. Chan WM, Lam DS, Lai TY, Tam BS, Liu DT, Chan CK. Choroidal vascular remodelling in centralserous chorioretinopathy after indocyanine green guided photodynamic therapy with verteporfin: Anovel treatment at the primary disease level. Br J Ophthalmol. 2003;87:1453–58.
8. Lai TY, Chan WM, Lam DS. Transient reduction in retinal function revealed by multifocal electroretinogram after photodynamic therapy. Am J Ophthalmol. 2004;137:826–33.
9. Tzekov R, Lin T, Zhang KM, Jackson B, Oyejide A, Orilla W. Ocular changes afterphotodynamic therapy. Invest Ophthalmol Vis Sci. 2006;47:377–385.
10. Ficker L, Vafidis G, While A, Leaver P. Long-term follow-up of a prospective trial of argon laserphotocoagulation in the treatment of central serous retinopathy. Br J Ophthalmol. 1988;72:829–34.
11. Khosla PK, Rana SS, Tewari HK, Azad RU, Talwar D. Evaluation of visual functionfollowingargon laser photocoagulation in central serous retinopathy. Ophthalmic Surg Lasers. 1997;28:693–7.
12. Tolentino MJ, McLeod DS, Taomoto M, Otsuji T, Adamis AP, Lutty GA. Pathologic features of vascular endothelial growth factor-induced retinopathy in the nonhuman primate. Am J Ophthalmol. 2002;133:373–85.
13. Seong HK, Bae JH, Kim ES, Han JR, Nam WH, Kim HK. Intravitrealbevacizumab to treat acutecentral serous chorioretinopathy: Short-term effect. Oph-

thalmologica. 2009;223:343–7.

14. Inoue M, Kadonosono K, Watanabe Y, Kobayashi S, Yamane S, Arakawa A. Results of one-yearfollow-up examinations after intravitrealbevacizumab administration for chronic central serouschorioretinopathy. Ophthalmologica. 2011;225:37–40.

15. Artunay O, Yuzbasioglu E, Rasier R, Sengul A, Bahcecioglu H. Intravitrealbevacizumab intreatment of idiopathic persistent central serous chorioretinopathy: A prospective, controlled clinicalstudy. Curr Eye Res. 2010;35:91–98.

16. Lim SJ, Roh MI, Kwon OW. Intravitrealbevacizumab injection for central serous chorioretinopathy. Retina. 2010;30:100–106.

17. Wang M, Munch IC, Hasler PW. Central serous chorioretinopathy. ActaOphthalmol. 2008;86:126–45.

18. Eandi CM, Ober M, Iranmanesh R. Acute central serous chorioretinopathy and fundus autofluorescence. Retina. 2005;25:989–93.

19. Ficker L, Vafidis G, While A, Leaver P. Long term follow-up of a prospective trial of argon laser photocoagulation in the treatment of central serous retinopathy. Br J Ophthalmol. 1988 Nov;72(11):829–34.

20. Avci R, Deutman AF. Treatment of central serous choroidopathy with the beta receptor blocker metoprolol (preliminary results) KlinMonblAugenheilkd. 1993 Mar;202(3):199–205.

21. Ober MD, Yannuzzi LA, Do DV, Spaide RF, Bressler NM, Jampol LM, Angelilli A, Eandi CM, Lyon AT. Photodynamic therapy for focal retinal pigment epithelial leaks secondary to central serous chorioretinopathy. Ophthalmology. 2005;112(12):2088–94.

22. Artunay O, Yuzbasioglu E, Rasier R, Sengul A, Bahcecioglu H. Intravitrealbevacizumab in treatment of idiopathic persistent central serous chorioretinopathy: a prospective, controlled clinical study. Curr Eye Res. 2010;35(2):91–8.

23. Lim JW, Kim MU, Shin MC. Aqueous humor and plasma levels of vascular endothelial growth factor and interleukin-8 in patients with central serous-chorioretinopathy. Retina. 2010 Oct;30(9):1465–71.

24. Avery RL, Pieramici DJ, Rabena MD, et al. Intravitrealbevacizumab (Avastin) for neovascular age-related macular degeneration. Ophthalmol. 2006;113:363–72.

25. Shahar J, Avery RL, Heilweil G, et al. Electrophysiologic and retinal penetration studies following intravitreal injection of bevacizumab (Avastin). Retina. 2006;26:262–9.

26. Stanga PE, Lim JI, Hamilton P. Indocyanine green angiography in chorioretinal diseases: indications and interpretation: an evidence-based update. Ophthalmol. 2003;110:15–21.

27. Piccolino FC, Borgia L. Central serous chorioretinopathy and indocyanine green angiography. Retina. 1994;14:231–42.

28. Torres-Soriano ME, Garcia-Aguirre G, Kon-Jara V. A pilot study of intravitrealbevacizumab for the treatment of central serous chorioretinopathy (case reports).Graefes Arch ClinExpOphthalmol. 2008;246:1235–9.

29. Seong HK, Bae JH, Kim ES. Intravitrealbevacizumab to treat acute central serous chorioretinopathy: short-term effect. Ophthalmologica. 2009;223:343–7.