

# EFFICACY OF BEVACIZUMAB IN CENTRAL SEROUS CHORIORETINOPATHY MANAGEMENT

Razaullah Khan,<sup>1</sup> Asad Aslam Khan,<sup>1</sup> Tehseen Mahmood Mahju<sup>1</sup>

## ABSTRACT

**Background:** Chronic central chorioretinopathy needs management so that morbidity may be controlled. **Objective:** To evaluate the efficacy of Bevacizumab in central serous chorioretinopathy. **Methodology:** It was a quasi experimental study. This study was conducted at Eye department of Mayo Hospital unit III, Lahore, Pakistan, from 1<sup>st</sup> September 2016 to 31<sup>st</sup> October 2017. Twenty three patients participated in this study. Sample was collected using non probability convenient sampling technique. Patients with chronic serous chorioretinopathy were included in this study and were administered Bevacizumab after three months of onset. SPSS version 23 was used to analyze the data. Frequency and percentage was calculated for the qualitative variables like gender and Paired test was applied to check the significant difference before and after the treatment on variables like visual acuity and central macular thickness. **Results:** There was complete resolution of Central Services Chorioretino-Pathy and reduction in the mean of central macular thickness after treatment measured through OCT and the difference between the two results was also statistically significant ( $p=0.001$ ). **Conclusion:** This study concluded that bevacizumab is significantly effective in the management of Central Services Chorioretino-Pathy. But more research work in the form of randomized controlled trails is suggested to evaluate the effectiveness of intravitreal bevacizumab in this condition.

**Keywords:** Bevacizumab, Chorioretinopathy, Visual acuity, Central macular thickness.

## INTRODUCTION

Central serous chorioretinopathy (CSCR) occurs most commonly in middle aged men with age ranging between twenty to fifty years.<sup>1,2,3</sup> Psychological stress and people having type A personality are prone to development of central serous chorioretinopathy.<sup>4</sup> Other risk factors include chronic use of corticosteroids, sympathomimetic agents, some psychopharmacological agents and endogenous high levels of corticosteroids. Poor vision and longer period of rehabilitation is associated with smoking.<sup>5</sup> When serous detachment occurs from choriocapillaris, through retinal pigment epithelium, this condition can be defined as central serous chorioretinopathy.<sup>6</sup> Choroidal neovascularization, tumors or inflammation are among the other causes of retinal pigment epithelium leakage, which need to be ruled out to make the final diagnosis of CSCR.

Serous chorioretinopathy has two distinct clinical presentations. Fluorescein angiography has been used to classify the cause of central serous chorioretinopathy by one or more particular secluded leak corresponding to the retinal pigment epithelium.<sup>7</sup> It has been well recognized by now that central serous chorioretinopathy can present as diffuse retinal pigment epithelial dysfunction, for instance, decompensated retinal pigment epithelium, chronic central serous chorioretinopathy and diffuse retinal pigment

epitheliopathy. Diffuse retinal epithelium dysfunction is characterized by neurosensory detachment of retinal epithelium, over areas of atrophy of epithelium and mottling of the pigment. Broad areas of granular hyper-fluorescence are seen on fluorescein angiography, which comprises areas of one or more leaks.<sup>8</sup>

Most common presentations of central serous chorioretinopathy are metamorphopsia, blurred vision, micropsia and mild dyschromatopsia.<sup>8</sup> Typical signs found on fundus examination are well demarcated detachment of retina at macula. Detachment of pigment epithelial can also occur in variable sizes, single or multiple. Sub retinal fluids can be turbid or fibrinous or clear. Sub retinal pigment epithelium space can also be occupied by the turbid fluid. Laser photocoagulation, photodynamic therapy and pharmacological agents like acetazolamide, mifepristone, propranolol and ketoconazole are different modes of treatment available for central serous chorioretinopathy.<sup>9</sup> Despite the availability of these treatment options, no modality of these agents has shown to reduce the reoccurrence and final visual acuity; instead these treatments only shorten the duration of symptoms.<sup>10</sup> Bevacizumab has anti permeability properties and thus thought to be effective in reversing the changes found in central serous chorioretinopathy.<sup>11</sup> It is a monoclonal antibody against vascular endothelial growth factor. The rationale of this study is as central serous chorioretinopathy is disease which leads to

1. Department of Ophthalmology, Mayo Hospital, Lahore, Pakistan.

eye sight loss, so it should be managed effectively. This study was conducted to evaluate the efficiency of Bevacizumab in treatment of central serous chorioretinopathy.

## METHODOLOGY

It was a quasi experimental Study, conducted in Ophthalmology Unit of Mayo Hospital, Lahore, from 1<sup>st</sup> September 2016 to 31<sup>st</sup> October 2017. Ethical approval was obtained from Hospital Ethics committee. Twenty three patients were included in this study. Sample was collected using non probability convenient sampling technique. Patient aged between 20 and 50 years, both genders and patients of chronic serous chorioretinopathy (CSCR) as per operational definition were included in this study. Patients with previous use of intravitreal bevacizumab, having choroidal neovascularization, more than 21 mmHg of intraocular pressure, history of thromboembolism, intraocular inflammation and retinal detachment were excluded from this study. All the patients included in this study, were presented in out-patient department of Mayo Hospital Lahore. Informed consent was ensured before including them in the study. Variables like, gender and age were recorded of each patient prior to the initiation of the study. Detailed anterior segment slit lamp examination, intraocular pressure measurement, dilated fundal examination and visual acuity was recorded at baseline and also at each follow up visit. Pre-operative OCT was done and macular thickness was documented. Injection was administered into the vitreal cavity using a 27G needle under topical anesthesia.

The patients were followed at 4 weeks intervals, fundus examination was done and resolution of central serous chorioretinopathy was recorded. Optical coherence tomography (OCT) was done at 4 weeks intervals for 3 months to assess the central macular thickness (CMT). After 4 weeks repeated injections were performed for persistent or recurrent central serous chorioretinopathy documented by optical coherence tomography imaging. Computer software SPSS version 23 was used to enter and analyze the data obtained from the procedure. Frequency and percentage was calculated for the qualitative variables like gender and Paired test was applied to check the significance and association among variables. P value less than and equal to 0.05 was taken significant.

## RESULTS

A total number of 23 patients were included in this study, belonging to both genders. There were 14 (60.87%) male and 9 (39.13%) females. Mean age was  $47.17 \pm 2.13$  years. The average uncorrected visual acuity was 0.5 using Log Mar visual acuity chart. The mean baseline value for visual acuity was  $42.82 \pm 7.91$ , while after treatment was  $57.78 \pm 4.33$ . The difference between the means of visual acuity at baseline and after treatment was statistically significant ( $p=0.000$ ). Similarly mean central macular thickness before and after treatment was  $357.89 \pm 96.17$  and  $249.76 \pm 30.19$   $\mu\text{m}$  respectively. There was reduction in the mean of central macular thickness after treatment and the difference between the two results was also statistically significant ( $p=0.000$ ) (Table-I).

**Table I: Outcome Variables before and after treatment**

Variable	Before Treatment	After Treatment	P . Value
Visual acuity	0.5	0.1	0.000
Central macular thickness ( $\mu\text{m}$ )	$357.89 \pm 96.17$	$249.76 \pm 30.19$	0.000

## DISCUSSION

There are multiple treatment options available for central serous chorioretinopathy like pharmacological agents (propranolol, acetazolamide and ketoconazole), laser photocoagulation and photodynamic therapy but none of these treatment options actually reduces the reoccurrence and improve visual acuity of the patients instead only have effect on symptoms of the central serous chorioretinopathy.<sup>11,12,13</sup> Intravitreal bevacizumab were administered in this study and the outcome in terms of visual acuity and macular thickness were analyzed. The results came out to be very promising and showed that intravitreal bevacizumab can be used as an effective treatment option for central serous chorioretinopathy.

The results of our study are in accordance to the results of the study done by Schaal KB et al<sup>13</sup> according to whom intravitreal bevacizumab can be regarded as an effective management option in the treatment of central serous chorioretinopathy. In another study, conducted by Torres-Soriano ME et al, found that all the patients who were treated with intravitreal bevacizumab had improvements in fluorescein angiographic leakage, visual acuity and resolved neurosensory detachment of retina.<sup>14</sup> Results of another study showed that, twelve patients

treated with intravitreal bevacizumab and eight patients treated with other treatment options had evidence of restored morphology at 6 months after treatment ( $p < 0.001$ ). They further described that vision was improved in patients who were treated with bevacizumab as compared to the others who were not, and also that central foveal thickness was also considerably lower after the treatment in these patients as compared to the patients who did not receive intravitreal bevacizumab ( $297 \pm 172 \mu\text{m}$  and  $174 \pm 68 \mu\text{m}$  respectively ( $P < 0.001$ )). These results clearly show that intravitreal bevacizumab although a novel treatment option yet can be used effectively in the treatment of selective groups of individuals suffering from chronic, persistent and idiopathic central serous chorioretinopathy.<sup>15</sup> In acute central serous chorioretinopathy, use of intravitreal bevacizumab may show quick improvement by reducing angiographic leakage and by resolving the neurosensory detachment. Studies have proved that intravitreal bevacizumab not only improves the condition of chronic central serous chorioretinopathy but has equal efficacy in acute central serous chorioretinopathy as well.<sup>16</sup> Recurrent cases of central serous chorioretinopathy can be effectively managed by the use of intravitreal bevacizumab as shown in a previous study.<sup>17</sup> Despite all these studies on the efficacy of bevacizumab as a treatment option, evidence on long term efficacy of this antibody is still scarce and studies show that it is associated with relatively lower risk of complications and improves vision and macular thickness.<sup>17</sup>

In contrast to the results of our study a Korean study has stated that in treating patients suffering from acute central serous chorioretinopathy, bevacizumab is not much effective as it has no helpful effect in severe settings when compared to a study group but it also showed that it had no adverse effects.<sup>18</sup> They emphasized on the fact that further investigations are required in order to establish the definitive role of bevacizumab as an option in central serous chorioretinopathy.<sup>18</sup> A randomized control trial was done to compare the efficacy of intravitreal bevacizumab and photodynamic therapy, which was in favor of the use of photodynamic therapy over intravitreal bevacizumab. Central foveal thickness was reduced more in patients who undergone photodynamic therapy as compared to the other

group which opted for intravitreal bevacizumab 53% and 25% respectively. Thus establishing the fact that intravitreal bevacizumab is not as much effective option of treatment as photodynamic therapy. Despite these results, they concluded that intravitreal bevacizumab is safe and effective treatment of central serous chorioretinopathy.<sup>19</sup> Among the many recent and previous studies, another study showed results in contrast to the results of the study just mentioned and their conclusion was that, foveal thinning and improvement in vision was more significant in group of patients managed with intravitreal bevacizumab as compared to those treated with low fluence photodynamic therapy.<sup>20</sup> In another study, a one year duration follow up was carried out on patients treated with intravitreal bevacizumab and the results were quite satisfactory in terms of treatment and outcome of central serous chorioretinopathy and thus concluded that intravitreal bevacizumab is an effective treatment for this chronic condition.<sup>21</sup>

## CONCLUSION

This study concludes that bevacizumab is effective in the management of chronic serous chorioretinopathy. But more research work in the form of randomized controlled trials is required to further evaluate the effectiveness of intravitreal bevacizumab in this condition.

### Conflict of Interest:

There was no conflict of interest regarding this study.

### Funding Source:

No extra funding source was used.

## REFERENCES

1. Witjaksana R, Sumual V. Treatment of Central Serous Chorioretinopathy with Carbonic Anhydrase Inhibitor. *Ophthalmological Indonesiana*. 2017 Feb 9; 42(2):121-7.
2. Nicholson B, Noble J, Forooghian F, Meyerle C. Central serous chorioretinopathy: update on pathophysiology and treatment. *Survey of ophthalmology*. 2013 Apr 30;58(2):103-26.
3. Tsai DC, Chen SJ, Huang CC, Chou P, Chung CM, Huang PH, Lin SJ, Chen JW, Chen TJ, Leu HB, Chan WL. Epidemiology of idiopathic central serous chorioretinopathy in Taiwan, 2001–2006: a population-based study. *PLoS One*. 2013 Jun 24;8(6):e66858.
4. Schubert C, Pryds A, Zeng S, Xie Y, Freund KB, Spaide RF, Merriam JC, Barbazetto I, Slakter JS, Chang S, Munch IC. Cadherin 5 is regulated by corticosteroids and associated with central serous chorioretinopathy. *Human mutation*.

- 2014 Jul 1;35(7):859-67.
5. Klein R, Lee KE, Gangnon RE, Klein BE. Relation of smoking, drinking, and physical activity to changes in vision over a 20-year period: the Beaver Dam Eye Study. *Ophthalmology*. 2014 Jun 30;121(6):1220-8.
  6. Liegl R, Ulbig MW. Central serous chorioretinopathy. *Ophthalmologica*. 2014;232(2):65-76.
  7. Quin G, Liew G, Ho IV, Gillies M, Fraser Bell S. Diagnosis and interventions for central serous chorioretinopathy: review and update. *Clinical & experimental ophthalmology*. 2013 Mar 1;41(2):187-200.
  8. Brandl C, Helbig H, Gamulescu MA. Choroidal thickness measurements during central serous chorioretinopathy treatment. *International ophthalmology*. 2014 Feb 1;34(1):7-13.
  9. Ezuddin NS, Lanza NL, Weng CY. Subthreshold micropulse laser photocoagulation in the management of central serous chorioretinopathy. *International ophthalmology clinics*. 2016 Oct 1;56(4):165-74.
  10. Fujita K, Imamura Y, Shinoda K, Matsumoto CS, Mizutani Y, Hashizume K, Mizota A, Yuzawa M. One-year outcomes with half-dose verteporfin photodynamic therapy for chronic central serous chorioretinopathy. *Ophthalmology*. 2015 Mar 31;122(3):555-61.
  11. Chung YR, Seo EJ, Lew HM, Lee KH. Lack of positive effect of intravitreal bevacizumab in central serous chorioretinopathy: meta-analysis and review. *Eye*. 2013 Dec 1;27(12):1339-46.
  12. Lim SJ, Roh MI, Kwon OW. Intravitreal bevacizumab injection for central serous chorioretinopathy. *Retina*. 2010 Jan 1;30(1):100-6.
  13. Schaal KB, Hoeh AE, Scheuerle A, Schuett F, Dithmar S. Intravitreal bevacizumab for treatment of chronic central serous chorioretinopathy. *Eur J Ophthalmol*. 2009 Jul 1;19(4):613-7.
  14. Torres-Soriano ME, García-Aguirre G, Kon-Jara V, Ustariz-González O, Abraham-Marín M, Ober MD, Quiroz-Mercado H. A pilot study of intravitreal bevacizumab for the treatment of central serous chorioretinopathy. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2008 Sep 1;246(9):1235-9.
  15. Artunay O, Yuzbasioglu E, Rasier R, Sengul A, Bahcecioglu H. Intravitreal bevacizumab in treatment of idiopathic persistent central serous chorioretinopathy: a prospective, controlled clinical study. *Current eye research*. 2010 Feb 1;35(2):91-8.
  16. Seong HK, Bae JH, Kim ES, Han JR, Nam WH, Kim HK. Intravitreal bevacizumab to treat acute central serous chorioretinopathy: short-term effect. *Ophthalmologica*. 2009;223(5):343-7.
  17. Lee ST, Adelman RA. The treatment of recurrent central serous chorioretinopathy with intravitreal bevacizumab. *Journal of Ocular Pharmacology and Therapeutics*. 2011 Dec 1;27(6):611-4.
  18. Lim JW, Ryu SJ, Shin MC. The effect of intravitreal bevacizumab in patients with acute central serous chorioretinopathy. *Korean Journal of Ophthalmology*. 2010 Jun 1;24(3):155-8.
  19. Lee JY, Chae JB, Yang SJ, Kim JG, Yoon YH. Intravitreal bevacizumab versus the conventional protocol of photodynamic therapy for treatment of chronic central serous chorioretinopathy. *Actaophthalmologica*. 2011 May 1;89(3):123-9.
  20. Semeraro F, Romano MR, Danzi P, Morescalchi F, Costagliola C. Intravitreal bevacizumab versus low-fluence photodynamic therapy for treatment of chronic central serous chorioretinopathy. *Japanese journal of ophthalmology*. 2012 Nov 1;56(6):608-12.
  21. Inoue M, Kadonosono K, Watanabe Y, Kobayashi S, Yamane S, Arakawa A. Results of one-year follow-up examinations after intravitreal bevacizumab administration for chronic central serous chorioretinopathy. *Ophthalmologica*. 2011;225(1):37-40.

**Article Citation:** Khan R, Khan AA, Mahju TM. Efficacy of Bevacizumab in Central Serous Chorioretinopathy Management. *JSZMC* 2018;9(3): 1463-66