Original Article

Comparison of Efficacy of Intravitreal Ranibizumab and Aflibercept in Central Serous Chorioretinopathy

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ABSTRACT

Aim: To compare the efficacy of Ranibizumab and Aflibercept in managing Central Serous Chorioretinopathy.

Study Design: Retrospective study.

Duration and Settings of the Study: This study was carried out at Bodla eye-care and Department of Ophthalmology at Combined Military Hospital (CMH) Multan on the record of patients having Central Serous Chorioretinopathy (CSCR) with a follow-up period from July 2022 to July 2024.

Methods: This study included 20 eyes of 20 patients with recurrent or chronic CSCR. All patients underwent vision assessment, fundus examination, and Optical Coherence Tomography (OCT) before and after treatment. Ten eyes received Ranibizumab (Patizra) 0.05 ml (0.5mg) and ten eyes received Aflibercept (Eylea) 0.05ml (2mg) single injection. The effectiveness was measured by improvements in the Best-Corrected Visual Acuity (BCVA) using Log MAR chart; and reduction in the Central Macular Thickness (CMT) evaluated by OCT.

Results: Initial BCVA for Ranibizumab-treated eyes ranged from 0.2 LogMAR to 1.0 LogMAR, with CMT between 250 and 560 microns. Aflibercept-treated eyes had baseline BCVA from 0.3 LogMAR to 0.7 LogMAR and CMT between 377 and 567 microns. After four to six weeks, BCVA improved to 0.0 LogMAR to 0.6 LogMAR in the Ranibizumab group, with CMT reduced to 198-421 microns. In the Aflibercept group, BCVA improved to 0.0 LogMAR to 0.5 LogMAR, with CMT reduced to 182-367 microns.

Conclusion: Both treatments significantly improved macular health in chronic CSCR patients. However, this study shows that Aflibercept has much better results with the standard dose as compared to Ranibizumab in the management of CSCR.

Keywords: Aflibercept; Best Corrected Visual Acuity; Central Macular Thickness; Central Serous Chorioretinopathy; Optical Coherence Tomography; Ranibizumab

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INTRODUCTION

After diabetic retinopathy, branch retinal vein occlusion, and age-related macular degeneration, Chronic Central Serous Chorioretinopathy (CSCR) is the fourth most prevalent retinopathy. CSCR is classified into three main types based on the duration and presentation: Acute (self-limiting, <3-6 months), Chronic (persistent, >6 months with retinal pigment epithelium (RPE) changes), and Recurrent (repeated episodes). It is generally associated with loss of central vision or contortion.[1] The condition occurs more frequently in men than women, with reported prevalence ratios ranging from 3:1 to 7:1, and is most often diagnosed between the ages of 30 and 51 years.[2] Before Anti-Vascular Endothelial Growth Factor (Anti-VEGF), the only treatment for Chronic CSCR used to be conservative photodynamic

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therapy or laser therapy and oral medications resulting in resolution of lesion in few weeks, or are months. However, some of the patients may end with macular damage causing defective vision & having complications like choroidal neovascularization and retinal atrophy. Previous studies on chronic CSCR have demonstrated that Aflibercept is an effective treatment option, showing improvements in BCVA and reductions in CMT.[3]

One or more focal leakage sites linked to decompensated RPE and RPE detachment are characteristics of chronic CSCR.[4] Three main theories have been proposed to explain its pathogenesis:

(i) Hyperpermeability of choroidal vascular system due to malfunctioning of the outer blood–retina barrier, (ii) impaired RPE function leading to reversed fluid transport, and (iii) Shedding of the outer photoreceptors that results in subsequent RPE damage.[5] Photodynamic therapy (PDT) remains the standard treatment for chronic CSCR and has demonstrated efficacy in persistent cases. Given that the pathogenesis of chronic CSCR involves choroidal hyperpermeability, Anti-VEGF agents have been proposed as a potential therapeutic option. However, current evidence on their effectiveness is limited. Studies had reported that Anti-VEGF therapy can significantly reduce thickness of the macula and promote subretinal fluid resolution in chronic CSCR, without any obvious negative consequences, when compared with Argon laser, micropulse diode laser photocoagulation, and PDT.[6,7]

Anti-VEGF medications have been suggested as a treatment for chronic CSCR in more recent times. Anti-VEGF therapies have been shown to be effective in managing conditions associated with intraretinal edema and subretinal fluid (SRF), including retinal vein occlusions, diabetic macular edema, and exudative age-related macular degeneration (ARMD).[8,9,10] Among the agents evaluated in multiple clinical trials are bevacizumab (Avastin) and aflibercept (Eylea). Early investigations, including results of Anti-VEGF therapy which have been reported through comparison studies, chart reviews, prospective and retrospective interventional case series in patients with chronic CSCR. Earlier Studies highlighted the significant role of lesion characterization in tailoring expectations and neovascular ARMD or CSCR under bevacizumab (or ranibizumab) therapy.[11,12]

Several diagnostic tests are available to confirm chronic central serous retinopathy and guide management. Fundus autofluorescence highlights areas of bright signal corresponding to serous retinal detachment, caused by accumulation of photoreceptor outer segments. OCT can demonstrate choroidal thickening and subretinal fluid. Fluorescein angiography and indocyanine green angiography localize areas of choroidal leakage and assist in treatment planning. Classic cases typically exhibit distinct leaks at the RPE level and little focused RPE damage, whereas diffuse retinal pigment epitheliopathy (DRPE) presents with diffuse leaking and extensive RPE impairment.[13,14] A bullous variation occurs in a small percentage of cases, characterized by inferiorly gravitating fluid leading to bullous serous retinal detachment.

A serous detachment of the neurosensory retina at the posterior pole, occasionally coupled with a serous RPE detachment, is the hallmark of chronic CSCR.[15] These results are easily identified and measured using OCT and are usually visible on slit-lamp biomicroscopy. Cystoid macular edema and intraretinal fluid may also appear in chronic situations. A single pinpoint leak at the RPE level is the most typical pattern on fluorescein angiography, while some patients may show several pinpoint leaks or the distinctive smoke stack pattern CSCR.[16,17] Another distinguishing hallmark is the presence of gravity-driven descending tracts of subretinal fluid, which can be seen on fundus autofluorescence (FAF) or fluorescein angiography. As RPE cells are harmed along the fluid pathway, these tracts first seem hyperautofluorescent but gradually become hypoautofluorescent. Consequently, chronic CSCR is best considered as a defect of the posterior pole rather than solely a maculopathy. Enhanced depth imaging (EDI) further demonstrates choroidal thickening.[18]

Before Anti-VEGF, the only treatment options for Chronic CSCR used to be conservative photodynamic therapy or laser therapy and oral medications. These may result in resolution of lesion in few weeks, or some months. However of the patients ended with macular damage causing defective vision. Complications like choroidal neovascularization and retinal atrophy may also be the Sequence. This study evaluated the efficacy of Anti-VEGFs Ranibizumab and Aflibercept in eye with chronic & recurrent CSCR.

METHODS

A retrospective study design was used on the record of 20 eyes of 20 patients with moderate to advanced CSCR at Bodla eye-care Hospital and the Department of Ophthalmology, CMH Multan. Both male and female patients were included with recurrent and chronic CSCR. Patients having different ocular diseases except CSCR were excluded in study. Eyes with ellipsoid zone disruption and with ocular or periocular infections, active ocular inflammation and patients with known hypersensitivity were also excluded.

All patients underwent VA assessment using Log MAR chart, 90-D dilated fundus eye examination and OCT (Optovue-Avanti). Ten eyes had Intravitreal Ranibizumab dose = 0.05ml (0.5mg) and remaining 10 eyes were treated with intravitreal Aflibercept dose = 0.05ml (2mg). Outcome measures were taken as improvement in best corrected visual acuity (BCVA) and CMT. We compared the records evaluated BCVA and CMT before and after months injections at 3 months (90th day).

Intravitreal injections were done in an operation theater under sterile conditions observing all antiseptic measures.

Topical anesthetic with Povidone-iodine using a 30-gauge needle, pulling the conjunctiva over the injection site with forceps or a sterile cotton swab to create a step-like entry path. After penetrating the sclera, the needle was advanced toward the center of the globe and the solution was gently injected into the mid-vitreous cavity. The needle was removed, and a sterile cotton swab was immediately placed over the injection site to prevent reflux. Post-injection povidone-iodine was used and topical antibiotics were given. IOP was also observed and treated as needed.

Paired-t test was used to compare the efficacy of both Anti-VEGFs before and after treatment. The data analysis was done using Statistical Package for Social Sciences (SPSS), Version 26.0.

RESULTS

Out of 20 patients, 13 were male with age ranged 25-45 years, and 7 female age ranged 20-35 years. The age of all participants ranged from 20 to 45 years. A paired-samples t-test was used to compare the average reduction in CMT and visual improvement in individuals with chronic CSCR, treated with intravitreal Ranibizumab and Aflibercept. The results were analyzed into two separate groups on the basis of efficacy or improvement of Anti-VEGFs. The mean CMT significantly decreased from 404.30 microns to 332.10 microns after treatment with Ranibizumab. This average reduction of 72.20 microns is statistically significant (p=0.003). Similarly, the findings with the use of Aflibercept showed there is substantial average reduction of 216.70 microns (p<0.01). The larger reduction in CMT with Aflibercept compared to Ranibizumab suggests that Aflibercept may be more effective in resolving the fluid buildup associated with CSCR.

Vision improved significantly after treatment with Ranibizumab. The mean visual acuity improved from 0.48 to 0.34 LogMAR with a mean difference of 0.14LogMAR (p = 0.004). This indicates that Ranibizumab effectively enhances visual acuity in CSCR patients. While, the mean visual acuity improved from 0.68 to 0.34 LogMAR, with a mean difference of 0. 22 LogMAR (p< .01) in Aflibercept injected eyes.

DISCUSSION

Before Anti-VEGF, the only treatment for recurrent and chronic CSCR used to be conservative resulting in resolution of the lesion in few weeks' months.

Findings from this study were that Aflibercept resulted in a greater reduction in CMT (216.70 microns for Aflibercept vs. 72.20 microns for Ranibizumab). Furthermore, Aflibercept also led to a more significant improvement in visual acuity. This notable improvement suggests that Aflibercept is highly effective in enhancing visual acuity in CSCR patients, with a greater improvement compared to Ranibizumab in which mean CMT decreased from 404.30 microns to 332.10 microns after treatment with Ranibizumab. This average reduction of 72.20 microns is statistically significant (p=0.003) indicating that Ranibizumab is effective in reducing fluid buildup under the macula in CSCR patients. Similarly, the findings with the use of Aflibercept showed there is a substantial average reduction of 216.70 microns having (p< .01). Findings from this study indicate that Aflibercep effectively enhances visual acuity in CSCR patients. While the mean visual acuity improved from 0.68 to 0.34 LogMAR, with a mean difference of 0.22 LogMAR (p < .01) for using Aflibercept.

This study showed that both Anti-VEGF treatments, Ranibizumab and Aflibercept, were effective in decreasing CMT and improving the BCVA in patients with chronic CSCR using a single injection with no recurrences. However, Aflibercept showed a more pronounced effect in both parameters compared to Ranibizumab. It is also suggested that patients with persistent CSCR may benefit from Anti-VEGF therapy as a primary treatment option. For individuals with chronic CSCR, we advise Anti-VEGF therapy if PDT is not accessible or access is lacking or contraindicated, if there is secondary choroidal neovascularization, or if they have failed conventional treatment with PDT and have persistent SRF.[19] Anti-VEGF injections should be contraindicated in patients with ocular or periocular infections, active ocular inflammation and patients with known hypersensitivity.[20]

CONCLUSION

Following intravitreal Anti-VEGF injections (Ranibizumab and Aflibercept), it was found that morphological changes in macula were very much improved. Both Anti-VEGF treatments, Ranibizumab and Aflibercept, were effective in decreasing CMT and improving the BCVA in patients with chronic CSCR. However, Aflibercept showed a more pronounced effect in both parameters compared to Ranibizumab.

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Conflict of Interest

Authors declare no conflicts of interest.

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AI Declaration

No artificial intelligence tools were used in the preparation of this manuscript.

Patient Consent:

Informed consent was obtained from all participants included in this study.

Ethical Approval

Ethics approval was obtained from the Institutional Review Board of CMH Institute of Medical Sciences (TW/51/CIMS-CMC, dated September 2024).

Authors' Contribution Statement

MAB: Conceptualization and design of the study, data acquisition, drafting, review and final approval of the final manuscript and agrees to be accountable for all aspects of the work.MAB: Conceptualization and design of study, data acquisition, data analysis and interpretation, drafting, review and final approval of final manuscript and agrees to be accountable for all aspects of the work. NHB: Conceptualization and design of study, data acquisition, data analysis and interpretation, drafting, review and final approval of final manuscript and agrees to be accountable for all aspects of the work. NS: Conceptualization and design of study, data acquisition, data analysis and interpretation, drafting, review and final approval of final manuscript and agrees to be accountable for all aspects of the work. AA: Conceptualization and design of study, data acquisition, data analysis and interpretation, drafting, review and final approval of final manuscript and agrees to be accountable for all aspects of the work. RR: Conceptualization and design of study, data acquisition, data analysis and interpretation, drafting, review and final approval of final manuscript and agrees to be accountable for all aspects of the work.

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