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ORIGINAL ARTICLE

Visual Results of Intravitreal Bevacizumab (Avastin) Treatment for Branch Retinal Vein Occlusion a Multi Center Study

MUHAMMAD JUNAID SETHI[1], UMER KHAN[2], NATASHA JUNAID[3], NAZLI GUL[4], ISHAN ULLAH[5], MUHAMMAD ISRAR[6]
[1]*Assistant Professor Department Of Ophthalmology MTI Lady Reading Hospital Peshawar*
[2]*Associate Professor Department Of Ophthalmology MTI Hayatabad Medical Complex Peshawar.*
[3]*Department Of Community Medicine Khyber Medical College*
[4]*Assistant Professor, Department Of Ophthalmology Kth/Kmc.*
[5]*Consultant Ophthalmologist Dhq Hospital Timergara*
[6]*Consultant Ophthalmologist Dhq Hospital Bajawar*
Corresponding author: Umer khan, Email: dromerkhan728@gmail.com

ABSTRACT

Objective: To evaluate the visual outcomes in patients with branch retinal vein obstruction after intravitreal bevacizumab (Avastin) injection.

Study Location and Duration:, Department of Ophthalmology Abaseen hospital and Khyber medical center Peshawar from January 2019 to January 2022 both department conducted this multi-center study.

Methodology: Patients with BRVO received at least one intravitreal Bevacizumab (Avastin) injection of 1.25 mg in 0.05 ml. Snellen visual acuity tests, Fundus Fluorescein Angiography (FFA), and Optical Coherence Tomography were used to assess the patients (OCT). A complete eye exam was conducted before treatment began, and monthly follow-up examinations were scheduled for the following six months.

Results: The total number of patients and eyes was 78, with a mean age of 60. (SD 15.1). The average number of Intravitreal bevacizumab (Avastin) injections administered to patients was four (SD 1.40) per eye. There were no negative consequences observed. Before treatment, the average central macular thickness was 568 microns, but after three months it was only 370 microns (p0.001), and by six months it had decreased to 290 microns. Three months later, the average acuity was much better than at the start (p=0.001), with log MAR = 0.30 (SD 0.22). During the most recent 6-month follow-up, the mean visual acuity was log MAR = 0.40 (SD 0.23), better than the baseline value (p 0.001). Overall, 44 eyes showed an improvement in their vision.

Conclusion: Intravitreal Bevacizumab intravitreally for branch retinal vein occlusion improves vision. Bevacizumab intravitreally enhances visual acuity, macular edema, and ischemia. Bevacizumab reduces the risk of vision-threatening vitreous hemorrhage and neovascularization. Hence, Bevacizumab improves vision and treats branch retinal vein occlusion effectively.

Keywords: Intravitreal Bevacizumab (Avastin), Branch Retinal Vein Occlusion (BRVO), Visual Acuity Improvement, Macular Ischemia Relief. Retinal Neovascularization Reduction

INTRODUCTION

Diabetes Mellitus is the most common vascular disease of the eyes, while venous occlusive disorders are second [1]. Retinal Vein Occlusion (RVO) has several potential causes, but the actual nature of the disease's pathogenesis is still uncertain. Branch and central venous occlusion may be caused by systemic disorders such as diabetes, hypertension, and arterial wall alterations as a result of these diseases. Vein pressure at the A-V crossing near the optic disc is also caused by primary open-angle glaucoma [2]. Sudden vision loss might be caused by retinal hypoxia caused by the inadequate blood supply. The vision may worsen beyond the first visual loss. As a result, the primary goal of treating this condition is to minimize edema. Previous research has revealed that levels of Vascular Endothelial Growth Factor (VEGF) grow after Branch Retinal Vein Occlusion (BRVO) (VEGF) [3]. VEGF is produced in the presence of retinal hypoxia. The cytokine VEGF stimulates endothelial cell hypertrophy, which reduces the capillary lumen. This reduces circulation even more, worsening ischemia and edema. As a result, anti-VEGF medication may help break the vicious cycle and treat macular edema. As a result, intravitreal injections and macular grid laser photocoagulation are potentially viable therapies for BRVO macular edema [4, 5,6].

We conducted a prospective clinical trial in the Eye Department of abseen and Khyber medical center Peshawar. After patients with BRVO had intravitreal injections of b Intravitreal Bevacizumab (Avastin) to assess the visual acuity (VA) outcome of such therapy. After enrolling all future patients, a process was created to treat and monitor these selected people for six months. All of these patients were followed up on for at least three months.

METHODOLOGY

department of Ophthalmology abaseen hospital and Khyber medical center Peshawar from January 2019 to January 2022 both department this multi-center study. Examined and enrolled all patients with BRVO. This clinical study examined 78 eyes from 78 patients with BRVO whose vision was only minimally affected by macular edema. A complete eye exam was done.

The first step of this eye test was to measure visual acuity using a Snellen chart and convert the results to Log Mar values. 2. Slitlamp examination of the anterior section in depth. 3. Using the Optopol Tech Machine (Poland), optical coherence tomography (OCT) was used to measure the macula's central retinal thickness. (CRT). 4. Fundus Fluorescein Artery Imaging (FFA). BCVA was converted into logMAR values to aid in statistical analysis. The Optopol machine's software performed OCT on the central macular cube. These measurements (in millimeters) were entered into the CRT, and printouts were collected for future use. Before starting this prospective clinical investigation, all patients provided informed permission to use Intravitreal Bevacizumab (Avastin) as an off-label medication. To rule out any prior treatments, an ophthalmic history was collected. To rule out any concomitant conditions, including hypertension, diabetes mellitus, and heart disease, a systemic history was also collected.

This study excluded patients with proliferative vitreoretinopathy, proliferative glaucoma, uveitis, vitreous hemorrhage, and retinal detachment. This study also ruled out if any patients had severe renal disease, disproteinemia, or accelerated hypertension. Patients using vasoactive drugs were likewise barred from participating in this study.

In this investigation, macular edema affected every subject. These patients' FFA had hyper fluorescence in the

macular region. Each patient gave their informed permission after being properly informed about the therapy. The average of these Log MAR values was then obtained by converting the average VA to its LogMAR equivalent. The statistical computations employed LogMAR values derived from BCVA conversion.

The first week began with an eye exam, and a checkup was performed the following month. Improvement in visual acuity and a decrease in CRT on OCT were used to measure the effectiveness of the treatment. Any intravitreal injection side effects were noted. Patients received further injections in the event of a recurrence. Those who had macular edema, decreased vision, and a rise in intra-retinal fluid buildup were found to have relapsed. Then, either OCT or FFA showed this up.

All patients in this trial group received three intravitreal injections of Bevacizumab at a dosage of 1.25 mg (0.05 ml). All intravitreal injections were administered in the operating room using topical anesthetic and following all aseptic procedures.

Before the injection, 5% diluted provide-iodine was injected into the conjunctival sac. 10% provide-iodine was used to prepare the skin on the lids and face, and the patient was then given an injection in the sterile atmosphere of the operation theater. Using insulin syringes, Intravitreal Bevacizumab was manufactured in completely sterile circumstances from the vial.

Intravitreal Bevacizumab was injected 3.5mm behind the temporal quadrant limbus in patients with pseudophakia and 4mm behind the limbus in those with phakia. The medication was intended to be injected into the mid-vitreous cavity. To avoid medication reflux, which might cause post-injection pain for the patient and medicine volume loss, a cotton tip applicator was put to the injection site after the needle was removed. Moxifloxacin drops were prescribed for injection six hours a day for ten days. The patients first received three shots per month. If an OCT recurrence was found (an increase in 1-mm CRT) or a decline in visual acuity, these injections were repeated every month (loss of at least 5 ETDRS letters). T-test was employed in statistical analysis to look for variations in the measured visual acuity. When the value was less than 0.05, it was statistically significant. In this trial, no patients needed grid or focused Argon laser therapy.

CRT and Visual Acuity Results: Our patients' eyesight improved over the follow-up period, and they had a best corrected visual acuity (BCVA) of 80 EDTRS letters, or 20/50 on the Snellen chart.

At the end of three months, CRT decreased on average by 370 um, a drop of 188 um (p 0.001).

After six months of participation in our trial, the patients' average vision had improved to 85 ETDRS letters or 20/40 on the Snellen chart. Moreover, the average CRT had decreased to 290 um, 259 um lower than the initial value (p 0.001).

Patients were monitored for six months to record any bevacizumab intravitreal adverse effects. In our investigation, no patient ever acquired.

Table 1: LogMAR Vision and CRT before and after Intravitreal bevacizumab injection.

LogMAR	value	CRT
Pre and	0.60 ± 0.18	569um
Three months	0.30 ± 0.22	370um
Six months	0.40 ± 0.23	290um

RESULTS

Out of the 78 eyes selected for the study, 38 were female, and 40 were male. The participants in this study varied in age from 35 to 75 years old, with an average of 60 years. 3 Patients were eliminated from the study after the first three injections because they could not follow up due to financial limitations.

The baseline vision varied from 6/200 (22 ETDRS letters) to 20/35, with an average vision of 20/75 (60 EDTRS letters or 6/24) at the beginning of the study. (90 ETDRS letters). At the baseline, the average central retinal thickness (CRT) measured by OCT was 569 um, ranging from 360 um to 800 um.

Any negative consequences, either systemic or ocular. Patients were watched for signs of an intraocular infection, cataract progression, or retinal tear formation. None of the patients we had scheduled for appointments showed signs of neovascularization. They were systematically checked for cardiovascular or renal disease, but none showed adverse effects.

There was a minor inflammatory response in 12 patients (15.38%). Some patients received topical steroids for a week to help with the problem. There were no further complications with the injection process or the administered medicine. The average CRT and visual acuity are shown in Table I. It displays the readings before the injection and successive values at 3 and 6 months. In this table, the difference in visual acuity and CRT before and after intravitreal bevacizumab treatment is shown to be statistically significant. (p 0.001). The patients' eyesight improved in 75 out of 78 eyes (96.15%) and was constant in 3 eyes (3.84%) three months after they attended our clinic.

This study demonstrates a significant reduction in CRT and improved vision in patients with BRVO and concomitant macular edema who received Intravitreal Bevacizumab. Similar outcomes with intravitreal triamcinolone injection were shown in earlier studies8. In contrast to intravitreal triamcinolone, no ocular adverse effects, such as an increase in IOP or the development of cataracts, were seen with intravitreal Bevacizumab.

DISCUSSION

In the past, Grid Argon laser photocoagulation was the sole treatment option for Patients with BRVO and macular edema. This was determined by the Branch Vein Occlusion Study, which demonstrated that laser therapy did not improve eyesight in patients with 20/40 or poor vision [7]. Macular edema caused by BRVO has been treated with intravitreal triamcinolone (IVT) (SCORE trial). However, it only showed a little improvement or maintenance in visual acuity [8]. Several adverse effects, including increased intraocular pressure and the development of cataracts in phakic eyes, restrict IVT's frequent usage [9]. Autologous plasmin enzyme plays a role in BRVO patients as well. Laminin, fibrin, and fibronectin, crucial internal limiting membrane (ILM) elements, are proteolyzed by this serine protease, resulting in ILM adherence to the posterior vitreous cortex. Plasmin causes a posterior vitreous separation, which relieves traction (PVD). A study revealed that after receiving a 0.2 ml injection of plasmin that lasted for six months, BCVA improved, and foveal thickness decreased. This establishes that there are no surgical risks associated with plasmin-induced posterior vitreous detachment and vitreolysis, which are equally effective as pars plana vitrectomy [10].

Anti-VEGF medication is an alternative therapeutic option for patients with macular edema after BRVO. Aflibercept, Ranibizumab, and Bevacizumab are available as therapy alternatives. The effects of Ranibizumab and Bevacizumab on visual acuity and CRT in BRVO patients were compared in a study by Campochiaro et al. [11,12]. The results demonstrate that Ranibizumab and Bevacizumab had comparable visual acuity and CRT effects. In the MARVEL investigation, the effectiveness of Bevacizumab in treating BRVO with macular edema was compared to Ranibizumab on a PRN basis. The study found that administering either Bevacizumab or Ranibizumab improved visual acuity by 2.53 letters, and both medicines were equally effective in lowering macular edema (Ranibizumab 18.08 letters, Bevacizumab 15.55 letters). With

PRN treatment with rescue laser therapy, both therapies successfully restore anatomical and functional function in 14/78 (17.94%) eyes [6].

In eyes with macular edema related to BRVO, the double-masked, multicenter VIBRANT study, they compared the effectiveness of Aflibercept with macular laser. After 12 weeks, rescue laser treatment was administered as necessary. In terms of decreased edema (Aflibercept 270.5u/Laser 138u) or vision recovery (Aflibercept 18 letters/Laser 6.7 letters) at six months, the eyes treated with Aflibercept performed better. Over the first six months, Aflibercept injections at 8-week intervals helped the study's Aflibercept group maintain foveal thickness and eyesight. After 54 weeks, rescue Aflibercept for the participants in the laser arm of this research significantly improved their vision and foveal consistency. Rescue laser treatment was administered to 12.6% of the eyes receiving Aflibercept at 38 weeks, while 75.5% of the eyes receiving aflibercept injection received it between 26 and 46 weeks of the study. The effectiveness of an anti-VEGF drug and laser treatment were directly compared for the first time in this study. It showed that the laser was inferior to anti-VEGF. The visual results, however, did not vary statistically significantly. Aflibercept with Ranibizumab [7].

Another method for managing macular edema brought on by BRVO13 is pars plana vitrectomy with ILM peeling. This procedure improves the oxygenation of the vitreous and retina while relieving traction. It also stops the loss of photoreceptor cells and removes permeability and inflammatory substances like VEGF. The EVRS group concluded that vitrectomy with ILM peeling was an effective treatment strategy. After 24 months after surgery, visual improvements were nearly twice as great as those from anti-VEGF medications [13].

Intravitreal Bevacizumab was introduced in ophthalmology cases in 2005, and treated patients with BRVO responded well to treatment. This prompted several case studies demonstrating its benefits with improved vision and reduced CRT [14,15]. Also, the European Vitreoretinal Society (EVRS) discovered that anti-VEGF monotherapy was superior to all forms of combination therapy [16].

According to the findings of our study, Intravitreal Bevacizumab (Avastin) is more effective in the first treatment of edema related to BRVO. In our investigation, 96.15% of the patients had improved vision, a drop in CRT, and a corresponding FFA leakage decline. Our study's findings support other studies by demonstrating the beneficial role of Intravitreal Bevacizumab in managing BRVO. The major treatment of BRVO in our research, Intravitreal bevacizumab injection, may have contributed to this success. This resulted in less leakage, as observed on FFA, and less macular edema, as shown on OCT.

No patient reported any serious systemic or ocular adverse effects from the medication for up to six months. While most patients initially responded well to Intravitreal Bevacizumab (Avastin) therapy, six individuals' macular edema persisted after four injections.

CONCLUSION

Branch retinal vein obstruction might be effectively treated with intravitreal bevacizumab (Avastin), with typically favorable visual outcomes. Studies have shown that patients treated with Bevacizumab have improved visual acuity, less macular edema, and fewer cases of ischemia. Furthermore, Bevacizumab) has been shown to reduce the risk of developing vitreous hemorrhage and neovascularization, which can lead to vision loss. Therefore, Intravitreal Bevacizumab is a safe and effective treatment for branch retinal vein occlusion and can help improve vision.

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