



### RESEARCH ARTICLE

## TO ASSESS REDUCTION IN MACULAR EDEMA BY SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY (SD-OCT) FOLLOWING INJECTION OF BEVACIZUMAB IN CASES OF CENTRAL RETINAL VEIN OCCLUSION (CRVO)

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### Manuscript Info

#### Manuscript History

Received: 10 June 2021  
Final Accepted: 14 July 2021  
Published: August 2021

#### Key words:-

Central Retinal Vein Occlusion, Macular Edema, Bevacizumab, Spectral Domain Optical Coherence Tomography

### Abstract

**Aim:** To study the reduction in macular oedema in Central Retinal Vein Occlusion cases following Intravitreal injection of Bevacizumab using Spectral Domain Optical Coherence Tomography.

**Methods:** 50 patients diagnosed with Central Retinal Vein Occlusion with macular oedema of more than 300 microns on Spectral Domain Optical Coherence Tomography (SD-OCT), who attended to Out patient Department of Government Regional Eye Hospital (GREH) between January 2020 to June 2020 were administered Intravitreal Injection of Bevacizumab (Avastin) 1.25mg in 0.05ml. Re-injections were given if SD-OCT showed persistence of macular oedema. In follow up visits, patients were evaluated with SD-OCT and Central macular thickness (CMT) was measured every month till 6 months from the date of first injection.

**Results:** Out of 50 cases included in the study, there was reduction in macular oedema in 45 (90%) cases and 5% had persistence of macular edema.

**Conclusion:** Intravitreal Bevacizumab is a safe and effective modality of treatment for reducing macular edema due to Central Retinal Vein Occlusion as per our study.

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### Introduction:-

Retinal vein occlusions (RVOs) remain the second most common sight-threatening vascular disorders after diabetic retinopathy. It is caused due to compression of retinal vein by arteriosclerotic artery resulting in turbulent venous flow leading to endothelial damage and thereby leakage of fluid and blood. The main cause of vision loss in RVO is macular oedema. VEGF has been implicated in the process of new vessel formation and increased vascular permeability. Of the VEGF receptor blockers in clinical trials and practice, Bevacizumab (Avastin, Genentech, Inc., San Francisco, CA), a full-length, humanized, monoclonal antibody directed against VEGF has gained popularity for treatment of macular edema. Originally used for metastatic colorectal carcinoma, this PAN-VEGF blocking monoclonal antibody was found to have beneficial effect in Retinal vein occlusion, Wet ARMD, Diabetic retinopathy. In Retinal Vein occlusions, the vascular changes are acute and hence even with single Anti-VEGF injection, there is significant reduction in Central macular thickness (CMT).

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**Aim of the study:**

To study the reduction in macular oedema in Central Retinal Vein Occlusion cases following Intravitreal injection of Bevacizumab, using Spectral Domain Optical Coherence Tomography (SD-OCT).

**Inclusion criteria:**

Patients attending the Retina clinic of GREH, Visakhapatnam, diagnosed with Central Retinal Vein Occlusion (CRVO) with Centre involving Macular Oedema with Central Macular Thickness (CMT) >300microns diagnosed by Optical Coherence Tomography(OCT)

**Exclusion criteria:**

Patients of age > 80 yrs  
 Patients suffering with Media opacities,  
 Macular edema due to other causes, like Diabetic retinopathy, CNVM etc.  
 Intraocular surgery within 1 month,  
 Vitreomacular traction,  
 Epiretinal membrane.

**Materials and Methods:-**

Study Design : Hospital based Interventional study

Study Period : January 2020 to June 2020.

Study Setup : Study conducted in Dept. of Ophthalmology , Government Regional Eye Hospital (GREH), Visakhapatnam

Sample Size : 50 eyes of CRVO satisfying the inclusion criteria

**Methodology:-**

An informed consent was obtained from the patient after informing the patient in detail regarding the off-labelled use of Intravitreal Bevacizumab and also regarding the entire treatment procedure and its possible beneficial outcomes and adverse affects and also the nature of the disease.

A detailed history was taken from the patient regarding the condition and a detailed General physical examination and Ophthalmological Examination was conducted.

Patients with macular oedema (CMT>300microns) due to CRVO received Intravitreal Avastin (IVA) injection 1.25mg in 0.05 ml duly following all the standard aseptic precautions.

Re-injections were given if OCT-Macula showed persistent or recurrence of macular oedema (ME) in follow-up visits.

Each patient was evaluated at subsequent follow-up visit every month till 6months from the day of first injection. The results were analyzed to see whether there was a significant change in CMT following the injection.

**Results:-**

A total of 50 eyes of 50 patients were included in the study. The maximum number of patients were in the age group of 61 to 70 years (68%). Table-1 shows the distribution of no. of patients in various age groups.

**Table1:-** No. Of Cases of CRVO in various Age Groups.

| Age Groups of the patients | No. of cases of CRVO | Percentages % |
|----------------------------|----------------------|---------------|
| <40yrs                     | 0                    | 0%            |
| 41-50yrs                   | 2                    | 4%            |
| 50-60yrs                   | 12                   | 24%           |
| 61-70yrs                   | 34                   | 68%           |
| >70yrs                     | 2                    | 4%            |
| Total                      | 50                   |               |

Of the 50 patients enrolled in the study, there were 33 males (66%) and 17 females (34%).Table-2 shows the Gender distribution of the patients.

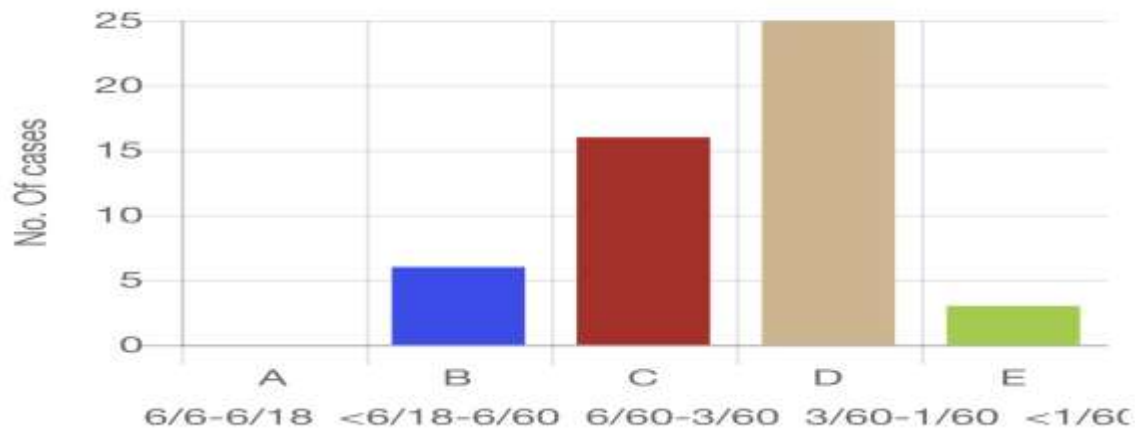
**Table-2:-** Gender Distribution.

|               | No. of Males | No. of Females |
|---------------|--------------|----------------|
| CRVO cases    | 33           | 17             |
| Percentages % | 66%          | 34%            |

Visual acuity of the patients at the time of presentation was recorded in Snellens and logMAR formats. Table-3 and Figure-1 show the Visual Acuity of the patients at the time of presentation in Snellens format in tabular and bar diagram format respectively.

**Table 3:-** Visual Acuity at presentation in Snellen's Format.

| VA<br>Visual Acuity | No. of patients of CRVO |
|---------------------|-------------------------|
| 6/6-6/18            | 0                       |
| <6/18-6/60          | 6                       |
| <6/60-3/60          | 16                      |
| <3/60-1/60          | 25                      |
| <1/60               | 3                       |
| Total               | 50                      |



The Central macular thickness of majority of cases at presentation was between 501-700 microns (64% of cases). Table-4 shows the macular thickness and number of patients.

**Table 4:-** Central Macular Thickness (CMT) and no.of cases of CRVO.

| CMT in microns | No.of cases of CRVO |
|----------------|---------------------|
| <300           | 0                   |
| 301-500        | 3 ( 6% )            |
| 501-700        | 32 (64% )           |
| 701-900        | 10 (20%)            |
| 901-1100       | 3 ( 6 % )           |
| 1101-1300      | 2 ( 4% )            |
| Total          | 50                  |

Table-5 shows the Mean reduction in CMT (Central Macular Thickness) for cases receiving the first injection within 1<sup>st</sup> month, 2<sup>nd</sup> month and 3<sup>rd</sup> month of presentation.

The maximum reduction in CMT was observed in cases receiving the first injection within first 1 month of presentation.

**Table 5:-** Mean CMT reduction after Intravitreal Anti VEGF.

| CRVO cases receiving first Bevacizumab injection | No. of cases | Mean CMT reduction after 6 months |
|--------------------------------------------------|--------------|-----------------------------------|
| Within 1 month of presentation                   | 32           | 255.6 mic                         |
| Within 2 months of presentation                  | 10           | 188.2 mic                         |
| Within 3 months of presentation                  | 8            | 101.6 mic                         |
| Total                                            | 50           |                                   |

The macular edema reduced in 45 cases and it persisted in 5 cases at the end of 6 months of follow up from giving the first injection. (Table-6)

**Table 6:-** No. of Cases with reduction and persistence of macular edema at the end of 6 months.

|                                  | CRVO |
|----------------------------------|------|
| Reduction in macular edema       | 45   |
| Persistence/ Recurrence of edema | 5    |
| Total                            | 50   |

The change in visual acuity in terms of log-mar units from the time of presentation to the time at the end of 6 months from the first injection are represented in Table-7. There was an improvement of 0.22 log mar units in terms of vision by the end of 6 months.

**Table 7:-** Change in Visual Acuity in logMAR Units before and after Intravitreal Injection of Avastin.

|      | At presentation      | After 6 months     |
|------|----------------------|--------------------|
| CRVO | 1.23 log mar (6/120) | 1.01 log mar(6/60) |

The improvement in visual acuity after giving three injections was more when the first injection was given within the first month of presentation compared to the first injection given after 1 month but within 3 months of presentation suggesting early intervention resulted in better visual outcomes. The change in mean visual acuity was 0.143 logMAR units with first injection given within the first month of presentation. The change in mean visual acuity was 0.051 logMAR units with first injection given after 1 month but within the first 3 months of presentation. (Table-8)

**Table 8:-** Change in Mean Visual Acuity in logMAR Units from the time of presentation and at the end of 6 months with first injection given within first month and after 1 month but within 3 months of presentation.

| No of injections and timing                                                               | Mean primary visual acuity at presentation | Mean final visual acuity at the end of 6 months of follow up | Change in mean visual acuity in log MAR units |
|-------------------------------------------------------------------------------------------|--------------------------------------------|--------------------------------------------------------------|-----------------------------------------------|
| 3 injections with first injection given within 1 month of presentation                    | 0.05                                       | 0.193                                                        | 0.143                                         |
| 3 injections with first injection given after 1 month but within 3 months of presentation | 0.04                                       | 0.091                                                        | 0.051                                         |

### Discussion:-

In the present study including 50 cases of CRVO, the mean age of presentation was 62.35 yrs. The Mean CMT in CRVO was 757.37 microns at presentation. The mean reduction of macular edema was maximum in patients who received the injection within first month of presentation and the reduction of CMT was 255.6 microns. The mean CMT decrease in CRVO after 1<sup>st</sup> injection of IVA was 152.75 microns and after 2<sup>nd</sup> injection of IVA was 134.6 microns and after 3<sup>rd</sup> injection of IVA was 90.7 microns.

According to **Shaaban A. Mahey<sup>1</sup>** study the mean age of the patients was 65.3 years  $\pm$  8.5 (range, 55–82 years). There were 20 males and 10 females patients in their study. The CMT reduction range was about 455 $\pm$ 126 to 356  $\pm$  118 microns. At the end of 6 months there was reduction of macular edema in 45 no. of cases (95%) of CRVO which

is similar to our study. Persistence or recurrence of macular edema implicates possibility of inflammatory mediators other than VEGF. The mean baseline VA was 20/240 (log MAR  $1.08 \pm 0.52$ ) in their study and it improved to 20/60 (log MAR  $0.48 \pm 0.32$ ).

According to **Joseph Pikkel study**<sup>2</sup>,

There was more reduction in mean CMT in patients receiving IVA within 1st month of presentation, which is similar to our study. In patients who received three doses of intravitreal injection of Avastin, there was better improvement in visual acuity in patients who received the first injection within 1 month of presentation compared to the patients who received the first injection after 1 month but within 3 months of presentation, which was similar to our study.

### **Conclusion:-**

Intravitreal Bevacizumab (IVA) was observed to be a safe and effective modality for treatment of macular edema in RVOs in reducing the CMT. However, more Randomised Controlled Trials with longer duration of follow up are required to establish the safety of the drug. The observed benefit was greater for patients in whom the first injection was administered early in the course of the disease.

### **Limitations of our study**

Relatively short-term follow-up period  
Small sample size  
Lack of a control group  
Off labelled use of the drug.

### **References:-**

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