

# A study of efficacy of grid photocoagulation combined with intravitreal bevacizumab for recurrent macular edema associated with branch retinal vein occlusion

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## Abstract

**Purpose:** To find out the effect of Grid Photocoagulation combined with Intra Vitreal Bevacizumab in Recurrent macular edema associated with Branch Retinal Vein Occlusion (BRVO). **Materials and Methods:** This descriptive type of observational hospital based study was conducted on the patients attending OPD block and Retina Clinic of Upgraded Department of Ophthalmology, SMS Medical College and Hospital, Jaipur. Patients underwent a single intravitreal bevacizumab injection (Avastin), followed by complete grid photocoagulation in single sitting. At 1 month and 3 month follow up patients underwent complete ophthalmological examination including BCVA, OCT and fundus angiography. Statistical analysis was done by using chi square test at alpha error 0.05 and power 80%. **Results:** After combined therapy (Intravitreal Bevacizumab with Grid photocoagulation), there was a significant decrease in foveal thickness when a comparison was done between baseline foveal thickness and foveal thickness at 1 and 3 months as denoted by the p-value. Significant improvement was also observed in BCVA at follow up after combined therapy (IVB with grid photocoagulation) at 1 month and 3 months when compared with baseline values with significant p-value. **Conclusion:** The current study finds that co-performing grid photocoagulation with IVB reduces the number of IVB needed in eyes with "recurrent macular edema associated with BRVO" and is hence an efficacious modality for its treatment.

**Key Words:** Grid Photocoagulation; Intravitreal Bevacizumab (IVB); Recurrent macular edema; Branch Retinal Vein Occlusion (BRVO).

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## INTRODUCTION

Macular edema remains one of the most common vision-threatening complication associated with retinal vascular diseases such as branch retinal vein occlusion (BRVO)<sup>1-4</sup>.

Today, vascular endothelial growth factor (VEGF) is known to play a major role in its pathogenesis by increasing capillary permeability<sup>5</sup>. The effect of anti-VEGF agents is rapid, albeit short<sup>6</sup> and we often see a recurrence of the macular edema after complete resolution brought about by the IVB<sup>7</sup>. Grid photocoagulation is an evidence-based treatment of the macular edema associated with RVO. In a report by the Branch Vein Occlusion Study Group<sup>8</sup> grid photocoagulation to macular edema caused by branch retinal vein occlusion (BRVO) significantly improved long-term visual prognosis. Grid photocoagulation does have long-term effects on the reduction of macular edema due to RVO, but it is sometimes difficult to perform effective coagulation in eyes that have severe macular edema. The rapid effect of IVB in reducing the macular

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thickening may allow clinicians to perform grid photocoagulation more effectively and safely. In the study described herein, we report both the effect and safety of grid photocoagulation in combination with IVB for recurrent macular edema associated with BRVO in terms of Foveal thickness and Visual acuity.

## MATERIAL AND METHODS

This was a descriptive type of observational hospital based study conducted on the patients attending OPD block and Retina Clinic of Upgraded Department of Ophthalmology, SMS Medical college and Hospital, Jaipur. Inclusion criteria was previously diagnosed branched retinal vein occlusion patients who have received prior (single or multiple) Intravitreal Bevacizumab and have documented evidence of complete resolution of cystic spaces and now presenting with decreased visual acuity due to recurrent macular edema (Recurrence of macular edema was defined as a relapse of the cystoid space at the foveal center and an increase of the foveal thickness to  $>250\text{ }\mu\text{m}$ ) and presently willing to participate in the study and giving informed consent. Vitrectomised eye, angle closure glaucoma or secondary glaucoma, eyes with epi-retinal membrane, age related macular degeneration, recent ocular infection or inflammation, conditions with hazy optical media, trauma, previous eventful cataract surgery, patients unwilling to participate were excluded. Patients confirming to the inclusion criteria were included in the study population and underwent a thorough systemic and ocular examination including best corrected visual acuity and ocular coherence tomography to obtain central foveal thickness which was taken as the baseline value. Patient underwent a single intravitreal bevacizumab injection (Avastin).

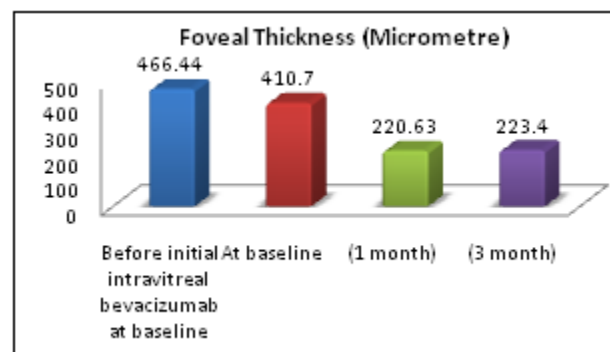
2-3 weeks later after clinical fundus examination with a 90D lens and indirect ophthalmoscopy with a 20D lens, patients underwent complete grid photocoagulation in single sitting (100 micro metre diameter spot, 0.1 second duration, medium white burn). At 1 month and 3 month follow up patient underwent complete ophthalmological examination including BCVA, intraocular pressure, fundus examination with indirect ophthalmoscopy, OCT and fundus angiography. BCVA and Central foveal thickness were recorded and analysis of the patients was done on the basis of these two parameters.

## OBSERVATIONS AND RESULTS

The maximum number of cases were in 51 to 60 age group (37%) followed by 61 to 70 years of age groups. The Mean age of the study population was  $58.93 \pm 9.92$  (24 to 80 years) and median was 59 years.

**Table 1: Foveal thickness Statistics**

| Foveal Thickness (Micrometre) | At Baseline | (1 Month) | (3 Month) |
|-------------------------------|-------------|-----------|-----------|
| N                             | 100         | 100       | 100       |
| Mean                          | 410.700     | 220.630   | 223.400   |
| SD                            | 103.92      | 36.39     | 50.17     |
| Minimum                       | 280.0       | 170.0     | 167.0     |
| Maximum                       | 743.0       | 344.0     | 400.0     |
| Median                        | 394.000     | 211.500   | 203.500   |

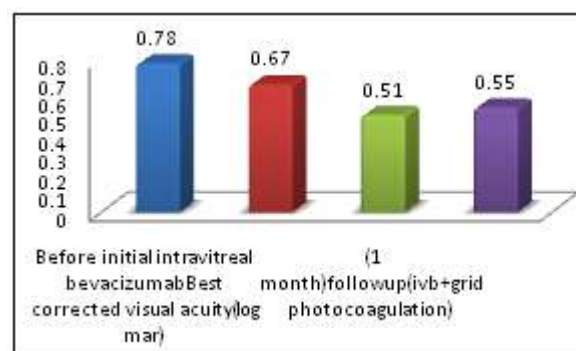


**Figure 1: Foveal Thickness (Micrometre)**

At Baseline the Mean foveal thickness (micrometer) of the study population was,  $410.7 \pm 103.92$  (280 to 743 micrometer) with median was 394.0. At 1 month,  $220.63 \pm 36.39$  (170 to 344 micrometer) with median was 211.5. At 3 month,  $223.63 \pm 50.17$  (167 to 400 micrometer) with median was 203.50.

**Table 2: Visual Acuity Statistics**

|         | Baseline | (1 Month) Followup (Ivb+Grid Photocoagulation) | 3 Month |
|---------|----------|--|---------|
| N       | 100      | 100  | 100     |
| Mean    | 0.67     | 0.51   | 0.55    |
| SD      | 0.22     | 0.15   | 0.21    |
| Minimum | 0.30     | 0.20   | 0.20    |
| Maximum | 1.60     | 1.00   | 1.30    |
| Median  | 0.60     | 0.50   | 0.50    |

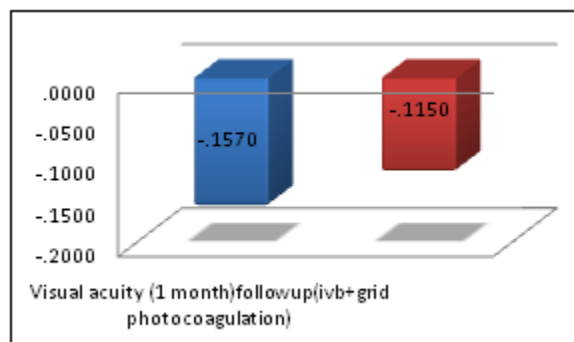


**Figure 2: Visual Acuity Statistics**

At Baseline The Mean visual Acuity of the study population was  $0.67 \pm 0.22$  (0.3 to 1.6 ) with median was 0.6 . At 1 month,  $0.51 \pm 0.15$  (1 to 0.5) with median was 0.5. At 3 month,  $0.55 \pm 0.21$  (0.20 to 1.3) with median was 0.50

**Table 3:** Paired Analysis of Visual Acuity from Baseline Visual Acuity (Log Mar)

| From visual acuity   | Baseline | Paired Differences |       |       |                       | p Value             |
|--|----------|--------------------|-------|-------|-----------------------|---------------------|
|  |          | Mean               | SD    | SEM   | 95% CI<br>Lower Upper |                     |
| Visual Acuity(1 month)<br>Follow up (ivb+grid<br>photocoagulation) |          | -.1570             | .1552 | .0155 | -.1878 -.1262         | <0.001; Significant |
| Visual Acuity (3 month)  |          | -.1150             | .1321 | .0132 | -.1412 -.0888         | <0.001; Significant |

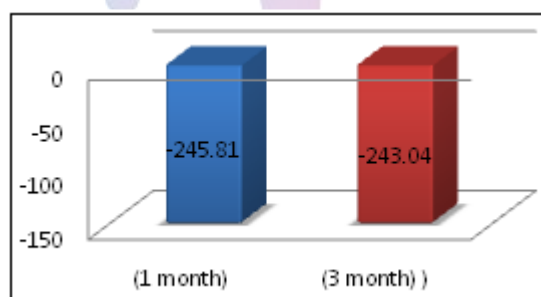


**Figure 3:** Paired Differences in visual Acuity

Significant improvement was observed according to Visual Acuity difference between Visual acuity (1 month) follow up (ivb+grid photocoagulation and Visual acuity (3 months) from baseline visual acuity(log mar) ( $P < 0.001$ )

**Table 4:** Paired Analysis of FOVEAL thickness

|  | Paired Differences Foveal thickness |        |       |         |         | p value             |
|--|-------------------------------------|--------|-------|---------|---------|---------------------|
|  | Mean                                | SD     | SEM   | 95% CI  |         |                     |
|  |                                     |        |       | Lower   | Upper   |                     |
| (1 month) - Baseline                               | -245.81                             | 108.81 | 10.88 | -267.40 | -224.22 | <0.01; Significant  |
| (3 month) – Baseline Foveal Thickness (Micrometre) | -243.04                             | 102.73 | 10.27 | -263.42 | -222.66 | <0.001; Significant |



**Figure 4:** Paired Differences Foveal Thickness from Baseline Foveal Thickness (Micrometre)

Significant improvement was observed according to foveal thickness difference between Baseline with 1 month and 3months ( $P < 0.001$ ).

## DISCUSSION

In present study, 100 patients of previously diagnosed Branch retinal vein occlusion who have received prior intravitreal bevacizumab and have documented evidence of complete resolution of cystic spaces and subsequently presenting with decreased visual acuity due to recurrent macular edema were included (Baseline). Recurrence of macular edema was defined as a relapse of the cystoid

space at the foveal center and an increase of the foveal thickness to  $>250 \mu\text{m}$ . The maximum number of patients were in 51 to 60 age group (37%) followed by 61 to 70 years of age groups suggesting that prevalence is more in older age group. The mean foveal thickness of the study population at the time of presentation was  $410.7 \pm 103.92$  (280 to 743 micrometer) (Baseline thickness) which improved to  $220.63 \pm 36.39$  (170 to 344 micrometer) at 1

month and  $223.63 \pm 50.17$  (167 to 400 micrometer) at 3 months after combined therapy (Intravitreal Bevacizumab with Grid photocoagulation). The foveal thickness improved significantly when a comparison was done between baseline foveal thickness and foveal thickness at 1 month and 3 months. The mean foveal thickness difference was  $-245.81$  and  $-243.04$  (micrometer) at 1 month and 3 months respectively ( $P < 0.001$ ). Ken Ogino *et al*<sup>9</sup> studied 19 eyes with Branch Retinal Vein Occlusion with macular edema and found that after combination therapy (intra vitreal bevacizumab followed by grid photocoagulation), foveal thickness was reduced significantly to  $276.7 \pm 90.9 \mu\text{m}$  in eyes with BRVO ( $P < 0.001$ ) at 1 month after treatment. Salah M Mady *et al*<sup>10</sup> conducted a study to assess the efficacy of intravitreal bevacizumab (IVB) combined with grid photocoagulation in the management of recurrent macular edema secondary to retinal vein occlusion. In this study grid photocoagulation was done followed by single injection of intravitreal bevacizumab. With this combination therapy, central macular thickness was reduced significantly to  $245.5 \pm 91.3 \mu\text{m}$  in eyes with BRVO ( $P < 0.001$ ) at one month. The Mean visual Acuity of the study population at the time of presentation (baseline) was  $0.67 \pm 0.22$  (0.3 to 1.6). Post Intravitreal Bevacizumab combined with Grid photocoagulation, mean visual acuity improved to,  $0.51 \pm 0.15$  (1 to 0.5) at 1 month and at 3 months,  $0.55 \pm 0.21$  (0.20 to 1.3). Significant improvement was observed in visual acuity at follow up after combined therapy (IVB with grid photocoagulation) at 1 month and 3 months when compared with baseline values ( $P < 0.001$ ). At 1 month mean visual acuity was  $-0.157$  and at 3 months it was  $-0.115$  respectively. Ken Ogino *et al*<sup>9</sup> studied that after combination therapy (intra vitreal bevacizumab followed by grid photocoagulation), visual acuity improved slightly to  $0.43 \pm 0.30$  in eyes with BRVO ( $P = 0.534$ ). Also at 1 month after treatment, 17 of the 19 eyes with BRVO showed complete resolution of the cystoid space. Salah M Mady *et al*<sup>10</sup> studied that visual acuity improved slightly to  $0.45 \pm 0.10$  in eyes with BRVO ( $P = 0.632$ ) at 1 month after combination therapy.

## CONCLUSION

The Branch Vein Occlusion Study Group recommended grid photocoagulation for macular edema associated with BRVO. However, an increasing number of recent reports show the efficacy of anti-VEGF therapy for macular edema secondary to RVO. While the effect of IVB is rapid, it is usually necessary for repeated injections to maintain the initial effect. Once the treatment has

stopped, recurrence may occur. In addition, repeated intravitreal injections of any anti-VEGF agent is associated with increased risk of systemic and ocular adverse effects. In the current study, we aimed to reduce the number of IVB in eyes with recurrent macular edema by co-performing grid photocoagulation. Additionally, by combining IVB with photocoagulation, we were able to produce burns with a relatively low laser settings. In present study, the combination therapy was performed for macular edema recurring after the effective previous IVB. This combination treatment reduced foveal thickness as effectively as did the previous IVB. Based on these findings, the current study concludes that co-performing grid photocoagulation with IVB reduces the number of IVB needed in eyes with “recurrent macular edema associated with BRVO” and is hence an efficacious modality for its treatment.

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