Comparison of the Safety and Efficacy of Intravitreal Ranibizumab with or without Laser Photocoagulation Versus Dexamethasone Intravitreal Implant with or without Laser Photocoagulation for Macular Edema Secondary to Branch Retinal Vein Occlusion

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Background: There is an ambiguity regarding the therapy of choice for patients with macular edema following branch retinal vein occlusion (BRVO).

Aim: The purpose of the study was to compare the efficacy and safety of ranibizumab (3 injections 0.5 mg) versus ranibizumab (1 injection 0.5 mg) with laser photocoagulation (LP) versus dexamethasone intravitreal (IVT) implant (0.7 mg) with or without LP in patients with macular edema following BRVO.

Materials and methods: 60 eyes of 60 patients were divided into 4 groups. Group 1 received IVT ranibizumab (3 injections 0.5 mg), Group 2 received IVT ranibizumab (1 injection 0.5 mg) + LP, Group 3 received dexamethasone IVT implant (0.7 mg), and Group 4 received dexamethasone IVT implant (0.7 mg) + LP. The endpoints were the difference in mean changes in best corrected visual acuity (BCVA), central macular thickness (CMT), and inter-group differences in contrast sensitivity (CS), retinal sensitivity (RS), and intraocular pressure (IOP).

Results: BCVA gains in Group 1 (18.00±8.51) patients were significantly (p < 0.05) higher than patients in Groups 2 (10.00±10.26), 3 (9.50±9.60), and 4 (10.50±10.97), after 6 months of therapy. No significant inter-group variation was found in the CMT, CS, and RS.

Conclusions: Ranibizumab (3 injections 0.5 mg) showed significantly higher BCVA gains at 6 months post-therapy. Improvements in the BCVA, CMT, CS, and RS were comparable initially in all the therapies.

Background

Macular edema following retinal vein occlusion is a major cause of visual loss.1 The incidence of branch retinal vein occlusion (BRVO) is almost three times higher than central retinal vein occlusion (CRVO).2 The pathogenesis of BRVO, though not completely understood, includes compression of the retinal vein at the arteriovenous crossing, degenerative changes of the vessel wall, and abnormal haematological factors.3 The increased expression of vascular endothelial growth factor (VEGF), prostaglandins, and interleukin-6 contribute to the development and progression of macular edema.4

Currently available therapies for macular edema secondary to BRVO include laser photocoagulation (LP), intravitreal (IVT) ranibizumab (Lucentis,
Genentech, San Francisco, CA, USA), dexamethasone IVT implant (Ozurdex, Allergan, Irvine, CA, USA), and aflibercept (Eylea, Bayer AG, Berlin, Germany).\textsuperscript{5} Bevacizumab and IVT triamcinolone are also sometimes used.\textsuperscript{6} However, no therapy is considered as the gold standard.

Ranibizumab, an anti-VEGF monoclonal antibody, is prescribed in single or multiple doses of 0.5 mg, with or without LP.\textsuperscript{7} Dexamethasone IVT implant, a corticosteroid, is prescribed in the dose of 0.7 mg with or without LP.\textsuperscript{8} First, there are no studies comparing the efficacy of the combination therapy of ranibizumab 0.5 mg single dose + LP with monotherapy of 3 doses of 0.5 mg ranibizumab. Second, there are a very few studies comparing the efficacy of the combination therapy of 0.7 mg dexamethasone IVT implant and LP versus 0.7 mg dexamethasone IVT implant monotherapy. Also, adequate head-to-head clinical trials comparing the efficacy of ranibizumab with dexamethasone IVT implant are lacking. Hence, the present study which was a prospective, quasi-randomized, open-label, controlled trial was undertaken.

**MATERIALS AND METHODS**

The present study was conducted from July 2014 to September 2016 following approval of the Institutional Ethics Committee of All India Institute of Medical Sciences, New Delhi. The present study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Inclusion criteria were BRVO patients of more than 40 years of age, with macular edema of at least 4 weeks duration, macular edema involving the foveal centre as observed by fluorescein angiography (Model VISUCAM 500, Carl Zeiss Meditec AG, Jena, Germany), vision reduced to 20/40 after best correction, and central macular thickness (CMT) > 250 μm as measured by optical coherence tomography (OCT) (Model CIRRUS HD-OCT, Carl Zeiss Meditec AG, Jena, Germany). Exclusion criteria were patients with previous vitreo-retinal surgery or laser therapy, media opacities which could interfere with investigative modalities/visualisation, use of intraocular/periocular steroids or anti-VEGF drugs in the past 3 months, diabetic retinopathy, stroke, glaucoma, and myocardial infarction.

Sixty eyes of 60 patients were divided into 4 groups. Group 1 (n = 15) received 3 doses of 0.5 mg IVT injections of ranibizumab at intervals of 4 weeks each. Group 2 (n = 15) received a single IVT injection of 0.5 mg ranibizumab followed by LP on day 7 of study. Group 3 (n = 15) received 0.7 mg IVT dexamethasone implant. Group 4 (n = 15) received 0.7 mg IVT dexamethasone implant followed by LP on day 7 of study. The selection of the therapy was based on the discretion of the treating practitioner under the assumption of similar efficacy as no proof of superiority of one therapy over the other is currently available, making the assignment quasi-random, even more so as several practitioners were involved. Patients were eligible for retreatment by LP after 4 months of completion of therapy if they met the criteria of CMT > 300 μm, best corrected visual acuity (BCVA) ≤ 20/40, and persistence of macular edema as observed by fluorescein angiography.

The parameters measured at baseline were BCVA by Early Treatment Diabetic Retinopathy Study (ETDRS) chart, CMT by OCT, contrast sensitivity (CS) by Pelli-Robson contrast sensitivity acuity chart, intraocular pressure (IOP) by applanation tonometry, and retinal sensitivity (RS) by microperimetry (Model MP-1, Nidek Inc., Gamagori, Japan). Retinal sensitivity was calculated within a circle of 500 μm on the fovea covering the central 4° field. Fluorescein angiography, slit lamp biomicroscopy, direct/indirect ophthalmoscopy, and clinical fundus photography (Model VISUCAM 500, Carl Zeiss Meditec AG, Jena, Germany) were also carried out as a part of the routine patient work-up process. After completion of therapy, patients from all four groups were called for follow-up visits at 1, 3, and 6 months and outcome parameters were re-evaluated. The primary endpoint was the change from baseline in the BCVA score after 6 months of therapy. Secondary outcome measures were change from baseline in CMT at 6 months, inter-group differences in the CS, RS, and IOP at 6 months.

For LP therapy, a double frequency Nd-YAG laser was applied in a grid pattern around the macula. The parameters observed while application of LP were spot size (50-100 μm), exposure (0.05-0.1 s), burn intensity (according to the diffuse retinal thickness), placement (1-2 burn-widths apart (500-3000 μm from foveal centre), and wavelength (green).

Statistical analysis was performed using SPSS-20 (IBM Inc., New York, NY, USA). Visual acuity was converted to the logarithm of the minimum angle of resolution (logMAR) scale for analysis. Values were expressed as mean ± standard deviation (SD). One way analysis of variance (ANOVA) was performed for inter-group comparisons. The level
The study was designed as a non-inferiority trial between any of the 4 treatment arms. The non-inferiority limit for the difference in the mean changes in visual acuity between the groups after 6 months of therapy was set as 5 letters. Assuming an α error of 5% and a power of 60%, with a true difference of 0.09 in the logMAR BCVA between any of the 4 arms and a SD of 0.13, the sample size was calculated to be 15 in each arm. The intention to treat principle was used for analyses and the last observation was carried out forward to impute for missing data.

RESULTS

The characteristics of the patients included in the study are shown in Table 1. There were no significant differences in the demographic or ocular characteristics of the study groups. The baseline outcome parameters in each group were comparable (Table 2). All groups showed a significant (p < 0.05) improvement in the BCVA, CMT, CS, and RS at 1, 3, and 6 months from baseline values, following therapy. Approximately 90% of the enrolled patients completed the study. One patient from Group 1, one patient from Group 2, two patients from Group 3, and two patients from Group 4 were lost in the follow-up.

The letters gained in the ETDRS chart from the baseline, after 1, 3, 6 months of therapy were 18.50±7.63, 16.50±7.91, and 18.00±8.51 in Group 1, 14.00±9.22, 10.50±9.22, and 10.00±10.26 in Group 2, 16.00±9.30, 13.00±9.22, and 9.50±9.60 in Group 3, and 17.50±9.71, 14.00±9.43, 10.50±10.97 in Group 4, respectively (Fig. 1). Inter-group comparison showed significantly (p < 0.05) higher BCVA gains in Group 1 as compared to Group 2, 3, and 4 after 6 months of therapy. There was no significant difference found in the BCVA gains of Group 2, 3 and 4 at all follow-up visits.

The difference in the CMT from the baseline at month 6 was 213.81±118.35 μm in Group 1, 193.27±106.89 μm in Group 2, 207.27±123.03 μm in Group 3, and 205.66±136.66 in Group 4. No inter-group significance was found in the reduction of the CMT from the baseline at 6 months of follow-up. The CMT in Groups 3 and 4 was considerably lower (non-significant) than Group 1 and 2 initially, at 1 and 3 months, following therapy (Table 2, Fig. 2).

Group 1 showed a trend towards significance (p < 0.07) than Groups 2, 3, and 4 in the CS, 6 months post-therapy. No significant inter-group difference was found in the CS between the groups 2, 3, and 4.

Table 1. Demographics and baseline characteristics of patients included in the four treatment groups for the management of macular edema following branch retinal vein occlusion

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, (years)</td>
<td>53.40±5.32</td>
<td>57.93±7.21</td>
<td>59.81±10.16</td>
<td>53.72±6.45</td>
</tr>
<tr>
<td>Sex, (number)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>7</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>8</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Hypertension, (number)</td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Blood pressure, (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>156.80±9.22</td>
<td>154.33±16.91</td>
<td>154.84±8.67</td>
<td>153.21±8.24</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80.23±5.33</td>
<td>82.41±9.54</td>
<td>81.23±6.14</td>
<td>83.33±8.21</td>
</tr>
<tr>
<td>Months from diagnosis</td>
<td>3.71±1.72</td>
<td>3.41±2.11</td>
<td>3.33±1.26</td>
<td>3.51±2.24</td>
</tr>
<tr>
<td>Best corrected visual acuity (logMAR/Snellen equivalent)</td>
<td>0.68±0.13 (6/30)</td>
<td>0.66±0.14 (6/30)</td>
<td>0.64±0.15 (6/24)</td>
<td>0.67±0.16 (6/30)</td>
</tr>
<tr>
<td>Central macular thickness, (μm)</td>
<td>487.53±105.90</td>
<td>491.47±92.01</td>
<td>493.67±100.79</td>
<td>488.93±120.61</td>
</tr>
<tr>
<td>Contrast sensitivity, (units)</td>
<td>1.03±0.23</td>
<td>1.12±0.25</td>
<td>1.02±0.45</td>
<td>1.11±0.38</td>
</tr>
<tr>
<td>Retinal sensitivity, (dB)</td>
<td>6.33±2.02</td>
<td>6.67±2.77</td>
<td>6.07±2.58</td>
<td>6.33±3.09</td>
</tr>
<tr>
<td>Intraocular pressure, (mm Hg)</td>
<td>12.46±2.45</td>
<td>12.60±1.84</td>
<td>12.20±2.54</td>
<td>12.73±2.12</td>
</tr>
</tbody>
</table>
Table 2. Outcome measures at different time intervals of patients included in the 4 treatment groups for the management of macular edema following branch retinal vein occlusion

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Groups</th>
<th>Baseline</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best corrected visual acuity (logMAR/ Snellen equivalent)</td>
<td>1</td>
<td>0.68±0.13 (6/30)</td>
<td>0.31±0.08 (6/12)</td>
<td>0.35±0.09 (6/15)</td>
<td>0.32±0.11 (6/12)*a,b,c</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.66±0.14 (6/30)</td>
<td>0.38±0.12 (6/12)</td>
<td>0.45±0.12 (6/19)</td>
<td>0.46±0.15 (6/19)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.64±0.15 (6/24)</td>
<td>0.32±0.11 (6/12)</td>
<td>0.38±0.13 (6/15)</td>
<td>0.45±0.12 (6/19)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.67±0.16 (6/30)</td>
<td>0.33±0.11 (6/12)</td>
<td>0.39±0.10 (6/15)</td>
<td>0.46±0.15 (6/19)</td>
</tr>
<tr>
<td>Central macular thickness (μm)</td>
<td>1</td>
<td>487.53±105.90</td>
<td>270.67±86.25</td>
<td>278.33±61.97</td>
<td>273.72±52.84</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>491.47±92.01</td>
<td>288.07±82.60</td>
<td>294.93±61.19</td>
<td>298.20±54.41</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>493.67±100.79</td>
<td>225.40±67.37</td>
<td>267.27±66.93</td>
<td>286.40±70.56</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>488.93±120.61</td>
<td>224.20±57.86</td>
<td>264.32±54.53</td>
<td>283.27±64.25</td>
</tr>
<tr>
<td>Contrast sensitivity (units)</td>
<td>1</td>
<td>1.03±0.23</td>
<td>1.78±0.22</td>
<td>1.72±0.18</td>
<td>1.60±0.13</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1.12±0.25</td>
<td>1.70±0.20</td>
<td>1.55±0.23</td>
<td>1.50±0.20</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.02±0.45</td>
<td>1.75±0.22</td>
<td>1.64±0.21</td>
<td>1.51±0.18</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.11±0.38</td>
<td>1.77±0.20</td>
<td>1.71±0.17</td>
<td>1.53±0.16</td>
</tr>
<tr>
<td>Retinal sensitivity (dB)</td>
<td>1</td>
<td>6.33±2.02</td>
<td>9.73±3.03</td>
<td>9.53±3.00</td>
<td>9.13±2.95</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>6.67±2.77</td>
<td>10.27±2.73</td>
<td>9.40±2.56</td>
<td>8.67±2.38</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>6.07±2.58</td>
<td>9.20±2.60</td>
<td>9.00±2.42</td>
<td>8.73±2.28</td>
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<tr>
<td></td>
<td>4</td>
<td>6.33±3.09</td>
<td>10.07±2.28</td>
<td>9.47±2.77</td>
<td>9.20±2.46</td>
</tr>
<tr>
<td>Intraocular pressure (mm of Hg)</td>
<td>1</td>
<td>12.46±2.45</td>
<td>13.27±2.05*b,c</td>
<td>12.93±2.46*b,c</td>
<td>12.47±1.88</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>12.60±1.84</td>
<td>13.47±1.68*d,c</td>
<td>13.07±1.94*d,c</td>
<td>12.80±2.08</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>12.20±2.54</td>
<td>16.33±2.41*b,d</td>
<td>15.47±1.73*b,d</td>
<td>12.93±2.19</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>12.73±2.12</td>
<td>16.00±3.25*c,e</td>
<td>15.85±2.31*c,e</td>
<td>13.20±1.86</td>
</tr>
</tbody>
</table>

One way ANOVA followed by multiple Tukey’s comparison test. Values are the mean ± SD, n = 15 in each group. *a = p value < 0.05 between Group 1 versus Group 2, *b = p value < 0.05 between Group 1 versus Group 3, *c = p value < 0.05 between Group 1 versus Group 4, *d = p value < 0.05 between Group 2 versus Group 3, *e = p value < 0.05 between Group 2 versus Group 4, *f = p value < 0.05 between Group 3 versus Group 4.

3, and 4 (Table 2). The RS showed no significant differences between Group 1, 2, 3, and 4 at all follow-up visits (Table 2). The IOP in Group 3 and 4 was significantly (p < 0.05) higher compared to the baseline values and also significantly higher than Group 1 and 2, at post-therapy follow-up visits of 1 and 3 months (Table 2). However, no significant (p < 0.05) inter-group variation was found in the IOP at 6 months.

By 6 months, 5 (33.33%) patients from Group 1, 6 (40.00%) patients from Group 2, 6 (40.00%) patients from Group 3, and 5 (33.33%) patients from Group 4 required rescue laser treatment.

**DISCUSSION**

The present study has observed the safety and efficacy of 3 IVT injections of ranibizumab (0.5 mg) monotherapy versus 1 IVT injection of ranibizumab (0.5 mg) + LP combination therapy versus dexamethasone (0.7 mg) IVT implant monotherapy versus combination therapy of dexamethasone (0.7 mg) IVT implant + LP.

The non-inferiority limit was set to 5 letters because this represents the test-retest variability for visual acuity. In the present study, ranibizumab (3 injections 0.5 mg) showed a mean difference of 8, 8.5, and 7.5 letters from ranibizumab (1 injection 0.5 mg) + LP, dexamethasone IVT implant (0.7 mg), and dexamethasone (0.7 mg) + LP, respectively, after 6 months of therapy. Although the...
Figure 1. Visual acuity in terms of ETDRS letters gained from baseline in the study groups at different time-points of follow-up.

Figure 2. Optical coherence tomography (OCT) images showing central macular thickness (CMT) of 1 patient from Groups 1 (A), 2 (B), 3 (C), and 4 (D) at baseline and at 6 months after therapy.
standard deviations in the visual gains were very large and ranged from 10.97 to 8.51 letters (due to the large variances), since the mean difference of > 5 letters was achieved by ranibizumab (3 injections 0.5 mg), it was considered to be a superior therapy than the others. No other treatment group besides ranibizumab (3 injections 0.5 mg) showed a mean difference of BCVA gains of > 5 letters from another group.

Ranibizumab is a recombinant, humanized, anti-VEGF monoclonal antibody, which prevents the binding of VEGF to VEGF receptors 1 and 2.9 Dexamethsone is a corticosteroid possessing anti-inflammatory and anti-angiogenic properties and is involved in inhibiting the expression of VEGF, and other pro-inflammatory cytokines such as interleukin-6 (IL-6), intercellular adhesion molecule 1 (ICAM-1), and monocyte chemoattractant protein 1 (MCP-1).10 Both pharmacological approaches address important factors in the pathogenesis of BRVO.

The ‘BRAnch retinal Vein Occlusion: Evaluation of Efficacy and Safety study’ (BRAVO), a high quality, double-blind, sham-controlled, randomized control trial, evaluated the efficacy of ranibizumab 0.5 mg and 0.3 mg. BRAVO revealed that 0.5 mg IVT ranibizumab significantly improved the BCVA as compared to the 0.3 mg ranibizumab group and the sham group, at the end of 6 months.11 Despite the differences in the study design, in comparison to BRAVO, the present study revealed that 3 doses of 0.5 mg ranibizumab significantly improved the BCVA versus a single dose of 0.5 mg RZB + LP, indicating an association of better visual outcomes in patients receiving multiple or a higher dose of ranibizumab.

The preliminary results of the ‘Efficacy and Safety of Ranibizumab With or Without Laser in Comparison to Laser in Branch Retinal Vein Occlusion (BRIGHTER)’ trial revealed that after 6 months of therapy, 3 injections of ranibizumab (0.5 mg) followed by PRN (pro re nata) regimen, caused a non-significant improvement in the BCVA as compared to the ranibizumab + LP combination therapy.12 The ‘Ranibizumab for Branch Retinal Vein Occlusion Associated Macular Edema Study (RABAMES)’, a 6 month, prospective, randomized clinical trial, concluded that LP combined with IVT ranibizumab neither enhanced functional and morphological improvement of IVT ranibizumab nor did it prevent or prolong recurrence of edema.13 A direct comparison of the present study to the BRIGHTER and RABAMES trials may not be possible due to their different study design. However, in contrast to the results of the BRIGHTER and RABAMES trials, the present study showed that the BCVA gains in the ranibizumab monotherapy group were better than the combination therapy of ranibizumab + LP, after 6 months of therapy. The lower dose of ranibizumab (single dose of 0.5 mg) used in the combination group of ranibizumab + LP may have attributed to this finding. A drawback of the present study was that the common dosing regimen of 3 IVT injections of 0.5 mg ranibizumab followed by PRN dosing was not followed in the present study. The PRN dosing regimen was not chosen after the initial loading doses of ranibizumab so as to minimize the drug costs.

A previous study comparing the efficacy of dexamethasone IVT implant with or without LP showed that the combination was synergistic in increasing the BCVA and lengthening the time between injections.14 In contrast, the present study did not show any significant difference in the outcome parameters between Groups 3 and 4, indicating no advantage of the combination of dexamethasone IVT implant + LP over dexamethasone monotherapy. The difference in the observations between the studies could be attributed to the different dosing regimens followed, wherein 3-12 dexamethasone IVT implants were administered over a span of 6 months in the previous study, whereas only 1 implant was administered in the present study. However, due to the low power of the present study, another drawback, larger and high power clinical trials are warranted to ascertain this observation.

The results of the ‘Global Evaluation of Implantable Dexamethasone in Retinal Vein Occlusion With Macular Edema (GENEVA)’ study showed that 0.7 mg dexamethasone IVT implant significantly improved the BCVA as compared to the sham treatment group.15 The ‘Efficacy and Safety of Ranibizumab Intravitreal Injections Versus Dexamethasone Intravitreal Implant in Patients with Branched Retinal Vein Occlusion (COMRADE-B)’ study directly compared the efficacy of 3 injections of 0.5 mg ranibizumab per month followed by the PRN regimen to 0.7 mg dexamethasone IVT implant. The COMRADE-B trial results revealed that the ranibizumab group showed significantly superior improvement in BCVA by 17.00±11.2 letters as compared to 9.1±12.5 letters in the dexamethasone IVT implant group at 6 months of follow-up.16 The GENEVA and COMRADE-B trials have different inclusion/exclusion criteria, study designs, and
dosing protocols than the present study. Hence, direct comparison may not be possible. However, the present study indicated a better outcome in the BCVA and CS, in the ranibizumab (3 injections 0.5 mg) treated group than the dexamethasone implant ± LP groups, aligning with the preliminary results of the COMRADE-B trial. The CMT in the dexamethasone IVT implant ± LP treated groups was considerably lower than the ranibizumab treated groups after 1 and 3 months of therapy. However, the initial superior (non-significant) CMT reduction could not be sustained by dexamethasone ± LP over the span of 6 months. Another previous study comparing the long-term efficacy of IVT ranibizumab versus dexamethasone IVT implant concluded that the ranibizumab treated patients showed a trend towards significance in the BCVA gains than dexamethasone IVT implant treated patients at the end of 12 months. Due to the relative short follow-up period, another drawback of the present study, the long term efficacy of dexamethasone IVT implant ± LP could not be determined. Multinomial and Bayesian comparison models also indicate a larger number of ranibizumab treated patients have improved visual outcomes than dexamethasone IVT implant treated patients.

Despite the ‘Branch Vein Occlusion Study (BVOS)’ proving the effectiveness of LP in the treatment of BRVO, the present study did not show any significant differences in the visual outcomes after adding LP to ranibizumab or dexamethasone IVT implant. The combination of ranibizumab (1 injection 0.5 mg) ± LP showed lower BCVA gains than ranibizumab (3 injections 0.5 mg) monotherapy. However, the lower dose of ranibizumab (single dose) in Group 2 could have influenced this observation. Dexamethasone IVT implant combined with LP showed similar endpoints as dexamethasone IVT implant monotherapy throughout the follow-up period of 6 months. The role of LP in BRVO needs reappraisal as suggested in previous reports.

The IOP of one patient in the dexamethasone IVT implant group and of one patient in the dexamethasone IVT implant combined with LP group was raised above 21 mm Hg and required topical antiglaucomatous drugs. None of the patients in ranibizumab ± LP groups had a raised IOP above 21 mm Hg or required antiglaucoma medications. No serious adverse drug reactions or development of cataract was observed in all of the investigated therapies. Thus ranibizumab ± LP groups appeared to be safer than dexamethasone IVT implant ± LP groups, combined with better visual outcomes. However, larger studies are needed to ascertain this finding.

The change observed in the CS and RS following ranibizumab/dexamethasone ± LP therapies is sparsely documented. CS refers to the ability of the visual system to distinguish between an object and its background. CS also helps characterize aspects of visual function that are not as well captured by visual acuity measurement such as reading performance, ambulation mobility, driving, and other tasks of daily living. The present study showed that the CS in ranibizumab monotherapy treated patients showed a trend towards significance after 6 months of therapy, as compared to the other therapies. However, a long-term evaluation of the CS could provide more certainty regarding the functional visual outcome of each of the therapies. The RS in all therapies showed significant gains from baseline values without any inter-group variations, following 6 months of therapy, in accordance with previous studies. The improvement in the RS may have been related to the to the restoration of the integrity of the foveal photoreceptor layer.

Another drawback of the present study was that the missing values were handled by the ‘last value carried forward’ method. This methodology could have attributed to a biased estimate of the treatment effect and could have underestimated the variability of the estimated result as the patients were lost in the follow-up. Also, since the method of allocating patients in the present study was not truly randomized, despite the precautions taken, the possibility of a selection bias cannot be ruled out. Furthermore, without the PRN regimen a considerable number of patients ranging from 33.33% to 40% required rescue laser therapy, making the inter-group comparison difficult. Since most patients could not afford the PRN regimen, rescue laser therapy was chosen as the economically suitable alternative for recurrent/persistent cases.

In conclusion, the study showed that ranibizumab/dexamethasone IVT implant ± LP are effective therapies for treating macular edema secondary to BRVO. However, the ranibizumab (3 injections 0.5 mg) monotherapy group showed a significantly higher improvement in the BCVA at the end of 6 months, as compared to other therapies. Despite causing a higher lowering in the CMT initially, dexamethasone IVT implant ± LP treated patients showed lower BCVA gains than the ranibizumab (3 doses) treated group at the end of 6 months. The
IOP was significantly higher in the dexamethasone IVT implant ± LP treated groups at follow-up visits of 1 and 3 months. No benefit was found in addition of LP to either IVT ranibizumab or dexamethasone IVT implant therapy.

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Сравнение безопасности и эффективности интравитреального ранибизумаба с лазерной фотокоагуляцией интравитреального импланта дексаметазона или без неё при макулярном отёке вторичном по отношению к разветвлёной окклюзии вены сетчатки

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Введение: Существует противоречие в отношении предпочтительной терапии для пациентов с макулярным отёком после разветвлённой окклюзии вены сетчатки (РОВС).

Цель: Цель исследования состояла в том, чтобы сравнить эффективность и безопасность ранибизумаба (3 инъекции по 0,5 мг) с ранибизумабом (1 инъекция по 0,5 мг) с фотокоагуляцией (ФК) с интравитреальным имплантатом дексаметазона (ИИД) (0,7 мг) с лазерной фотокоагуляцией (ЛФ) или без неё у пациентов с макулярным отёком после РОВС.

Материалы и методы: 60 глаз 60 пациентов были разделены на 4 группы. Группе I был введён ранибизумаб (3 инъекции по 0,5 мг), группе 2 - ранибизумаб (1 инъекция 0,5 мг) + ЛФ, группе 3 - имплантат дексаметазона ИИД (0,7 мг) и группе 4 - имплантат дексаметазона ИИД (0,7 мг) + ЛФ. Конечными точками были различия в средних изменения наилучшей коррекции острой зрения (НКОЗ), центральной толщины макулы (ЦТМ) и контрастной чувствительности (КЧ), чувствительности сетчатки (ЧС) и внутриглазного давления (ВГД).

Результаты: Улучшение РОВС у пациентов 1-ой группы (18,00 ± 8,51) было значительно (р <0,05) выше, чем у пациентов 2-ой группы (10,00 ± 10,26), 3 (9,50 ± 9,60) и 4-ой (10,50 ± 10,97) через 6 месяцев после начала лечения. Никаких внутригрупповых изменений не было обнаружено в ЦТМ, КЧ и ЧС.

Выводы: Ранибизумаб (3 инъекции по 0,5 мг) показал значительно большее улучшение при РОВС через 6 месяцев после начала терапии. Улучшения НКОЗ, ЦТМ КЧ и ЧС были изначально сопоставимы при всех видах терапии.