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A Prospective Study on Clinical Efficacy of Intravitreal Bevacizumab and Macular Grid Laser in Patients with Macular Edema Secondary to Branch Retinal Vein Occlusion

Soumyadeep Hazra [a#ω*] and Tapes Kanti Saha [a≡ω]

[a] *Jagannath Gupta Institute of Medical Sciences and Hospital, Budge Budge, Kolkata, West Bengal, India.*

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Branch retinal vein occlusion (BRVO) is the second most common cause of retinal vascular abnormality after diabetic retinopathy. Persistent macular edema develops in 60% of eyes with BRVO. Untreated, only 14% of eyes with chronic macular edema will have a visual acuity (VA) of 20/40 or better. If not resolved spontaneously, treatment is necessary in the form of intravitreal injection of Anti-VEGF followed by Macular Grid Laser. Bevacizumab is the Anti-VEGF of choice in developing countries because of its prolonged action and cheap price, which helps in preventing neovascularisation and thus further haemorrhages. Laser helps in stopping the leakage and thus helps in treating the macular edema.
Aims and Objectives: The aim of the study is to evaluate the efficacy of intravitreal Bevacizumab and Macular grid laser in the management of macular edema secondary to Branch Retinal Vein Occlusion in patients attending the ophthalmology.
Materials and Methods: In this research study, 32 patients presenting with macular edema secondary to Branch Retinal Vein Occlusion to ophthalmology OPD were included after taking their

[#] *Senior Resident;*
[≡] *Assistant Professor;*
[ω] *Dr.;*
**Corresponding author: E-mail: soumyadeep.hazra@gmail.com;*

consent and the study was carried out for a period of 2 years. Detailed history taking, Visual acuity, slit lamp examination, Fundus examination and OCT were done for all before treatment and also during every follow ups. FFA was done before treatment and after 3 months of laser. As treatment, all of them were given intravitreal injection of bevacizumab followed by macular grid laser.Patients were followed up on Day 1, Day 4, Day 7 and 4 weeks after intravitreal injection and 3 months after grid laser.

Results: In our study out of 32 patients, 17 were male (52%) and 15 were females (48%). The average age of the patient was 59 (range 40-70). The commonest co-morbidities in the patients were either Diabetes or Hypertension or both. The commonest type of BRVO was superotemporal BRVO. The average visual gain was statistically significant. The average decrease in Central Macular Thickness was 383 microns and this was statistically significant ($p<0.05$). There was no serious ocular or systemic complications following intravitreal injection of Bevacizumab in our study

Conclusion: In the management of macular edema secondary to Branch Retinal Vein Occlusion Intravitreal Bevacizumab injections in combination with subsequent macular grid treatment significantly improves vision and reduces macular edema.

Keywords: Branch retinal vein occlusion; vascular endothelial growth factor; macular edema; intravitreal injection; bevacizumab; avastin; macular grid laser; central macular thickness; diabetes mellitus; hypertension.

1. INTRODUCTION

Branch retinal venous occlusion is a common cause of visual loss mostly due to macular edema and is often associated with diabetic retinopathy [1,2]. It can be ischaemic or non-ischaemic based on extent of capillary perfusion [3]. There are multifactorial diseases with several risk factors such as age, hypertension, atherosclerotic retinal vein changes, diabetes mellitus, hyperhomocystinaemia and open angle glaucoma [3].

The major stimulus in the development of macular edema is the hypoxia induced production of Vascular Endothelial growth factor (VEGF) which increases permeability and results in retinal edema as well as neovascularisation [4].

Fundus Flouroscein Angiography (FFA) shows change in vessel permeability, and helps to identify areas of macular edema, neovascualrisation and non perfusion [3]. Optical Coherence Tomography helps in analyzing cross sectional images of macula which is an important diagnostic and prognostic tool in the management of macular edema secondary to Branch Retinal Vein Occlusion. It also helps to detect the morphological patterns in all types of macular edema in vein occlusions in the absence of dense media opacities [5].

Laser photocoagulation being the standard management for BRVO, in a report by the Branch Vein Occlusion Study Group, 10 grid photocoagulation to macular edema caused by branch retinal vein occlusion (BRVO) significantly improved long-term visual prognosis [6]. Macular grid laser has been recommended in case of macular edema and visual acuity worse than 6/12 but has a risk of causing inadvertent macular burn. Hence newer modalities like anti VEGF agents have been studied for the treatment of BRVO [7]. The anti VEGF agent Ranibizumab (Lucentis) has been approved by US FDA for treatment of macular ededma secondary to BRVO [8]. Another anti VEGF agent Bevacizumab (Avastin) has been used extensively as an off-label drug for the management of BRVO and has been found to be equally effective [9,10] and is much more cost effective.

The Branch Vein Occlusion Study (BVOS) recommends laser treatment after 3 months of onset to avoid the harmful effects of laser in those who may recover spontaneously and to allow haemorrhages to clear up sufficiently to get a reliable Fundus Fluorescein Angiography and to do effective laser photocoagulation [6]. Anti VEGFs can be given even in the presence of retinal haemorrhages and the ocular complications associated with it are very rare [11]. Presently it is not possible to predict which group of patients will resolve spontaneously and hence prolonged observation for spontaneous resolution may not be advisable when an effective and safe modality of treatment is available. There is evidence to suggest that early treatment with intravitreal Bevacizumab may lead to better visual outcome for macular edema

secondary to BRVO as compared to deffered treatment [12].

2. METHODS

This is a Randomized prospective interventional study done for a period of two years which consists of 32 patients with macular edema secondary to branch retinal vein occlusion fulfilling the inclusion and exclusion criteria, attending the outpatient department of Jagannath Gupta Institute of Medical Sciences and hospital. Each patient was be studied for a period of 3 months.

2.1 Inclusion Criteria

1. Patients are selected irrespective of sex
2. Age >40 and <70 years
3. Fresh cases of BRVO with macular edema attending the outpatient department. (Fresh cases are defined as patients with BRVO presenting for the first time to the hospital and diagnosed at the institute or if diagnosed elsewhere have not undergone any treatment. Macular edema was defined as Central Macular Thickness greater than 250 microns with evidence of cystic spaces on Optical Coherence Tomography).

2.2 Exclusion Criteria

Systemic exclusion criteria:

1. Coronary artery disease
2. Stroke
3. History of any thromboembolic events
4. Anticoagulant therapy

Ocular exclusion criteria:

1. Old BRVO
2. Patients with glaucoma
3. Pregnant or lactating women.
4. Neovascularization of the iris or neovascular glaucoma in the study eye
5. Hazy media due to corneal opacity, cataract or uveitis
6. Patients with central retinal vein occlusion.
7. Patients who have undergone laser or anti-VEGF/ steroid injections.

Data will be collected from the patient after informed consent. Patients fulfilling the inclusion and exclusion criteria will be taken.Detailed examination of both eyes will be done by various methods like visual acuity with snellens chart, near vision by Jaegers chart, best corrected visual acuity by streak retinoscopy, Slit lamp bio-microscopy, amsler grid test, Fundus examination by direct, indirect ophthalmoscopy, +78 D and +90 D lens, Intraocular pressure by Goldmann applanation tonometry, Optical coherence tomography- spectral domain, Fundus photograph, Fundus fluorescein angiography after 3 months of treatment.

A complete medical history for any of the following disorders were obtained: Diabetes mellitus, Renal disease, Hypertension, Coronary arterial disease, Cerebro-vascular disease, Systemic or ocular medications. All patients were referred for a consultation by physician.

For intravitreal injection of Bevacizumab, the patients eye were anaesthetized with topical anaesthetic drops of 0.5% paracaine and then a drop of 5% povidone iodine was instilled into the eye and waited for 30 seconds. eye was painted with 5% povidone iodine taking special care to paint the margin of the eyelids and base of eyelashes.Then the eye was draped with sterile surgical towels and eye ball was exposed using wire speculum and irrigated with ringer lactate including the conjunctival sac using 10 ml syringe.The eye was held with a Lim's forceps and the point of injection marked using a Castravejo Callipers at a distance of 3.5 mm from the limbus for pseudophakic eye and 4mm from the limbus for phakic eye in the superotemporal quadrant. At the marked site, the intravitreal injection was given through pars plana route with a 30-gauage needle mounted on the tuberculin syringe containing 1.25mg in 0.05 ml of Bevacizumab. Following the injection Indirect Ophthalmoscopy was done to look for central arterial pulsations. Paracentesis was done and the eye was patched .The patient was instructed to remove bandaged after 4 hours. Topical Eye Drops moxifloxacin 0.5% six hourly, Topical Eye Drops Prednisolone acetate 1% thrice a day and Topical Eye drops brimonidine 0.2% twice a day were administered for seven days after injection. Patients were instructed to return immediately in case of ocular pain, redness or deterioration of vision. Follow up visits were scheduled on Day 1,Day 4, Day 7, 4 weeks following injection.

The macular grid laser was done under topical anaesthesia using one drop of 2% xylocaine and burns are placed with the help of 532nm Nd Yag Green laser and Mainster Lens, in a grid pattern over the area of diffuse edema with each burn

spaced by 1 burn width apart beginning 500 m from the foveal avascular zone and extending to the edge of the macular edema, but not further peripheral than the large arcade vessels avoiding the foveal avascular zone. Patient is reviewed after 3 months.

On each visit the following were assessed: Visual acuity, slit lamp examination, dilated fundus examination, Optical Coherence Tomography (OCT).

The results of these 32 patients each were collated, tabulated and analysed and subjected to statistical analysis. To study about the efficacy, visual acuity was checked after 1st, 2nd and 3rd injections and after laser and measurement of IOP were performed at 1, 3 and 6 months. Macular condition and Central macular thickness on OCT was observed and documented.

The data was subjected to statistical analysis using Unpaired T test on Epi info software from http://www.cdc.gov/epiinfo.

3. RESULTS

In this recent study, it is observed that among 32 patients, most of them were male and was from a age group of 56-60 years.

In our study, it is seen that most of the patients (81%) were having any comorbidity, either diabetes mellitus or hypertension or both.

Table 1. Age and sex distribuition

Age range (years)	Male number %		Female number %		Total number %	
40-45	02	06%	01	04%	03	09%
46-50	01	04%	01	04%	02	06%
51-55	02	06%	02	06%	04	13%
56-60	07	21%	05	16%	12	37%
61-65	03	09%	03	09%	06	19%
66-70	02	06%	03	09%	05	16%
Total	17	52%	15	48%	32	100%

Table 2. Comorbidities

Comorbidities	Number	Percentage(%)
Diabetes Mellitus	10	31%
Hypertension	02	06%
DM + Hypertension	14	44%
No Comorbidities	06	19%
Total	32	100%

Table 3. Type of BRVO

Type of BRVO	Number	Percentage(%)
ST BRVO	19	59%
IT BRVO	13	41%
SN BRVO	00	00%
IN BRVO	00	00%
Total	32	100%

[ST- superotemporal; IT- inferotemporal; SN- superonasal; IN- inferonasal]

Table 4. Laterality

Eye involved	Number	Percentage (%)
Right Eye	17	53%
Left Eye	12	38%
Both Eyes	03	09%
Total	32	100%

Table 5. Visual acuity at different stages of study

Visual acuity	VA-P	VA-1	VA-2	VA-3	VA-L
< 6/60	07(21.8%)	06(18.7%)	06(18.7%)	04(12.5%)	01(3.1%)
6/60 – 6/36	12(37.5%)	13(40.6%)	11(34.4%)	13(40.6%)	08(25.0%)
6/36 – 6/24	11(34.4%)	10(31.2%)	12(37.5%)	12(37.5%)	17(53.1%)
6/24 – 6/12	02(6.3%)	03(9.4%)	03(9.4%)	03(9.4%)	06(18.7%)

[VA-P → Visual Acuity at preliminary presentation.
VA-1 → Visual Acuity after 1st injection of Bevacizumab.
VA-2 → Visual Acuity after 2nd injection of Bevacizumab.
VA-3 → Visual Acuity after 3rd injection of Bevacizumab.
VA-L → Visual Acuity after Macular Grid Laser.]

Most of the patients in this study were having superotemporal BRVO(59%) followed by that of inferotemporal BRVO (41%).

It is seen, right eye is most involved eye (53%), whereas few had involvement of both the eyes (09%).

In this recent study, it is seen that during primary presentation before any treatment, most of the patients had a visual acuity ranging from 6/36-6/60 (37.5%), followed by that with a vision of 6/24-6/36 and 7 patients had a vision worse than 6/60 (21.8%). After giving intravitreal injection of bevacizumab, it is seen that there is a slight decrease in the number of patients who had visual acuity less than 6/60 (3.12%) with increase in the number of patients with visual acuity ranging from 6/12-6/24 by 3.12%. After second injection, there was a increase in the number of patients with vision ranging from 6/24-6/36 by 6.25% with a reduction in the number of patients with 6/36-6/60 vision. With the third injection, it was evident about the efficacy of the injection in improving visual acuity with reduced number of patients with visual acuity less than 6/60 by 3.12% and increased number in the group with better vision. After three injections, macular grid laser was done, after which there was significant decrease in the number of patients with vision less than 6/60 by 9.37% and with vision of 6/36-6/60 by 15.62%.There was significant increase in the number of patients with vision more than 6/36 by 25%.

In our study, it is observed that with first injection of bevacizumab there was a reduction in the number of patients belonging in the group of central macular thickness of more than 700 microns with a decrease in the mean CMT by 73 microns. This same trend was maintained with the second and third injection leading to reduction of CMT in most of the patients (90.62%) less than 700 microns with a significant decrease of mean CMT by 236 microns after third injection from that after first injection. There was a total fall in the number of patients with CMT more than 600 microns after laser and most of them (66%) had CMT ranging between 200-400 microns. There was a reduction in the mean CMT from 415 to 268 microns after laser by 147 microns.

Table 6. Central macular thickness (CMT) at different stages ostudy

CMT (in microns)	CMT-1	CMT-2	CMT-3	CMT-L
200-400	01(3.1%)	02(6.3%)	10(31.2%)	21(65.6%)
400-600	06(18.7%)	09(28.12%)	12(37.5%)	11(34.4%)
600-700	12(37.5%)	12(37.5%)	07(21.8%)	00(0.0%)
700-800	10(31.2%)	08(25.0%)	03(9.4%)	00(0.0%)
800-900	02(6.3%)	01(3.1%)	00(0.0%)	00(0.0%)
900-1000	01(3.1%)	00(0.0%)	00(0.0%)	00(0.0%)
Mean value (in microns)	651	578	415	268

[CMT-1 → Central Macular Thickness after 1st injection of Bevacizumab
CMT-2 → Central Macular Thickness after 2nd injection of Bevacizumab.
CMT-3 → Central Macular Thickness after 3rd injection of Bevacizumab.
CMT-L →Central Macular Thickness after Macular Grid Laser.]

4. DISCUSSION

In our study, the average age of onset of BRVO being 59 years and the youngest being of 40 years, which matches the same of Hayreh et al. study. The mean age of male and female patients are 58 and 60 years respectively which correlates with that of Hamid et al. study. In our study, the number of males and females affected are 52% and 48% respectively which is not in accordance with a study conducted by Simsek et al.

Among the 32 patients included in the study, 44 % had combined diabetes and hypertension, 31% had only diabetes and 6% had only hypertension. Diabetes and hypertension seems to be the most prevalent comorbidity associated with BRVO. Superotemporal BRVO appears to be the most common type of BRVO in my study, around 19 patients, followed by inferotemporal temporal BRVO ,13 patients.

In our study, it is seen that during first presentation, most of the patients fall in the group of visual acuity of less than 6/36 (59.4%). After first intravitreal injection, it is seen there is reduction in number of patients with visual acuity less than 6/60 by 3.1%, with a subsequent increase in the visual acuity which after second and third injection changed significantly, increasing the number of patients (78.12%) with visual acuity ranging from 6/24 to 6/60. After laser treatment, due to improved visual acuity, maximum number of patients had a vision more than 6/24 (72%).

In this study, the mean central macular thickness at presentation was 651 microns, which reduced to 578 microns after 1st injection , to 578 microns after 2nd injection ,to 415 microns after 3rd injection and to 268 microns after laser.

These findings are comparable with the following studies (both visual acuity and macular edema)

A. BVOS study concluded that compared with the control group in which the mean improvement from baseline was 0.23 lines and 37 % gained ≥2 lines, in the laser group the mean improvement from baseline BCVA was 1.33 lines (about seven letters) and 65 % gained ≥2 lines [13].
B. The BRAVO study 63 reported that the mean gain from baseline at month 6 was 16.6 letters in patients receiving 0.3 mg of ranibizumab, 18.3 letters in those receiving 0.5 mg, and 7.3 in those receiving sham injection. 59 and the median percent reduction in excess foveal thickness was 337.3 (97%) in 0.3 mg group, 345.2 (97.6%) in 0.5-mg group and 157.7 (27.9%) in sham.
C. Sivakami A Pai et al study showed marked short term improvement of vision and reduction of macular edema following intravitreal injection of Bevacizumab in most patients [14].

The prevalence and five year incidence of BRVO according to Beaver Dam Eye Study was 0.6%. The pathological process at the site of vascular occlusion consists of degenerative changes in the vessel wall, abnormal blood constituents and stasis of blood flow, together they are known as Virchow's Triad. They are interrelated and play an important role in thrombogenesis [15]. Patients with BRVO present with visual complaints ranging from no visual complaints to severe visual loss. Patient with macular involvement often present with sudden onset of blurred vision and metamorphopsia , or a relative visual field defect [16]. Relative Afferent Pupillary Defect is seen in case of ischaemic BRVO. In acute cases, fundus examination shows dilated tortuous veins, flame shaped haemorrhages, dot and blot haemorrhages, retinal edema, cotton wool spots whereas chronic cases presents with signs of venous sheathing, cystoid macular edema, micro aneurysms, collaterals, shunt formation, hard yellow exudates, cholesterol crystal mottling of retinal pigment epithelium. Retinal neovascularisation usually develops in the first 6-12 months [17,18,19].

Macular edema is the most sight threatning complication of BRVO which may be accompanied by neovascularisation, retinal detachment, subretinal scarring, macular scarring [20].

FFA in BRVO shows variable delayed venous filling, blockage by blood, staining of the vessel wall, hypofluorescence due to capillary non perfusion and pruning of vessels in the ischaemic area. It accurately defines the retinal vascular characteristics that may have prognostic significance like macular edema, macular non perfusion and large segments of capillary non perfusion [21,22].

OCT acts as a prognostic tool to measure the central macular thickness before, during and

after treatment to check whether the edematous thickened macula is getting reduced or not.

Grid macular laser can be effective in reducing diffuse macular edema caused by branch retinal vein occlusions or by diabetic maculopathy. Adequate treatment of the maculopathy results in obliteration of the microvascular lesion, resolution of edema, absorption of hard exudates and stabilization or improvement of visual acuity. It has chances of causing foveal burn or severe choroidal neovascularisation.

In branch vein occlusions, retinal hypoxia occurs in the distribution of the occluded vein and may elicit a neovascular response in the affected area. Sector panretinal photocoagulation is then the treatment of choice. In addition, macular edema may develop and may be successfully treated with focal laser photocoagulation, resulting in vision improvement. Due to occluded venules, there is increased hydrostatic capillary pressure which leads to capillary leakage and thus to cystoid macular edema. According to Arnarsson and Stefansson grid-laser ablation of the photoreceptors of the outer retina reduces overall oxygen consumption of the outer retina and permits oxygen to diffuse more readily from the choroid to the vasculature of the inner retina. The increased diffusion raises oxygen tension in the inner retina and relieves hypoxia. Additionally, this increase in oxygen tension causes autoregulatory vasoconstriction and resistance in the arterioles. In turn, hydrostatic pressure in the capillaries and venules is reduced, causing constriction (Laplace‘s Law) and shortening of neighbouring venules and arterioles. Such constriction and shortening of arterioles and venules will decrease the fluid flow from the intravascular space into the surrounding tissue and therefore reduce tissue edema (Starling‘s Law) [23].

Normally laser light is absorbed by the pigment of the retinal pigmented epithelium and converted to heat resulting in damage to photoreceptors with sparing of the overlying retina. If there is intraretinal blood where laser is delivered, hemoglobin absorbs the laser light and converts it to heat in the inner retina resulting in a superficial burn, which may damage ganglion cells and their axons, causing a permanent scotoma and reducing the damage in the photoreceptor layer thereby failing to reduce oxygen utilization by photoreceptors—the objective of the treatment. Also, compared with DME, the leakage in BRVO is more confluent, involving telangiectatic retinal vessels in the half of the macula on the side of the occlusion.

The vascular endothelial growth factors (VEGFs) are considered as key molecules in the process of angiogenesis and macular edema. VEGF have been shown to trigger the breakdown of blood retinal barrier and growth of new vessel, which may leak blood and fluid into eye following retinal ischaemia. These leaky blood vessels may contribute to macular edema and neovascularisation of retina and iris [24]. One possible stratergy for treating macular edema is to inhibit VEGF activity by competitively binding VEGF with a specific neutralizing anti-VEGF antibody. Avastin (Bevacizumab), Lucentis (Ranibizumab) and Macugen (Pegaptanib) are recently introduced anti –VEGF drugs used in management of diabetic retinopathy , wet ARMD and BRVO [25]. The proposed mechanism of action of anti- VEGF agents are regression of existing abnormal microvasculature, normalizing of surviving mature vasculature and inhibition of vessel growth and neovascularisation [26]. Both ranibizumab and bevacizumab block all isoforms of VEGF. Bevacizumab has a considerably longer half life , which may be worrisome given the systemic absorption after intravitreal injection. On the other hand, the larger size and longer half life (17-21 days) of bevacizumab also give it some distinct advantages over ranibizumab (half life 3 days). Its dosing scheme may last longer, thereby requiring fewer injections, and ranibizumab has only 1 binding site for VEGF while bevacizumab has two [27,28]. The complications of bevacizumab included infection, retinal detachment, raised IOP, floaters, cataract.

There are many other anti-VEGF available options, but due to its prolonged action, fewer injections and less cost, bevacizumab is a better option in our country, even though other options hold more chances of better vision after treatment than bevacizumab. Thus, if other more effective anti-VEGF options can be made available for people from every socioeconomic strata, that will help us to serve the people with BRVO and macular edema, gaining more effective vision who are unable to afford those better options recently. Moreover, further studies can help to come up with better and more economic options with better results.

Further studies need to be concentrated on reducing the number of injections more efficiently, reducing the chances of injection-

induced infection but increasing the efficacy. Any future studies must concentrate more on the economic condition of our country where most of the patients are unable to afford the most effective option and thus compromising visual prognosis for the same.

5. CONCLUSION

Retinal Vein Occlusions are the second most common retinal vascular cause of reduced vision second only to diabetic retinopathy. The standard care for Branch Retinal Vein Occlusion is focal grid laser for macular edema and scatter laser photocoagulation for neovascularisation. The use of anti- VEGFs in management of complications of BRVO has been approved. Intravitreal injection of Bevacizumab leads to improvement of vision and reduction of macular edema which can be monitored by Optical Coherence Tomography.

In our study, it is evident that in the management of macular edema secondary to Branch Retinal Vein Occlusions, intravitreal injection with Bevacizumab followed by macular grid laser once haemorrhages resolves, has shown marked improvement in the visual acuity after 2-3 injection. This was also associated with significant reduction in the central macular thickness. The mean improvement in vision was significant with a shift of maximum patients to the group of visual acuity ranging from more than 6/24 from less than 6/36 and reduction in mean central macular thickness on OCT was 383 microns and this was statistically significant ($p<0.05$). The drug appears to be well tolerated and has not shown any safety concerns in our study.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

An informed written consent was obtained from all patients. Every patient received an explanation of the purpose of the study. All participants' data were confidential with secret codes and in a private file for each patient. Research results were only used for scientific purpose.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERRENCES

1. Cugati S, Wang JJ, Rochtchina E, et al. Ten-year incidence of retinal vein occlusion in an older population: the Blue Mountains Eye Study. Arch Ophthalmol. 2006;124:726-32.
2. Hayreh SS. Retinal vein occlusion. Indian Journal of ophthalmology. 1994:42 (3):109-132.
3. Leibreich R. Ophthalmoskopische Notizen (3.Apoplexia retinae). Arch Ophthalmologic. 1855;1:346-351.
4. Somesh A, Puja B, Rekha, Sonali S, Neha D. Spectral Domain OCT Patterns Of Macular Edema Associated With Branch Retinal Vein Occlusion In Indian Eyes; NJIRM. 2013;4(6):102-106.
5. Argon laser photocoagulation for macular edema in branch vein occlusion. Amj Ophthalmology. 1984;98:271-282.
6. The Branch Vein Occlusion Study Group, ―Argon Laser Photocoagulation for Macular Edema in Branch Vein Occlusion,‖ American Journal of Ophthalmology. 1984;98(3):271-282.
7. FDA Submission tracking Number BLA 125156/053. Approval dated 22 Jun 2010 addressed to Genentech, Inc.
8. Priglinger SG, Wolf AH, Kreutzer TC, Kook D, Hofer A, Strauss RW, et al. Intravitreal Bevacizumab injections for treatment of central retinal vein occlusion : six month results of a prospective trial. Retina. 2007;27(8):1004-12.
9. Kreichbaum K, Michels S, Prager F, Georgopoulos M, Funk M, Geitzenaue W, et al. Intravitreal bevacizumab for macular edema secondary to retinal vein occlusion: 12 month results of a prospective clinical trial. Br J Ophthalmol. 2009;93:453-456.

10. Goatman KA. A reference standard for the measurement of macular edema. Br J Ophtahlmol 2006;90(9):1197-1202.
11. Florian R, Jost BJ, Ulrich HN, Spandau. Early intrvitreal bevacizumab for Non-Ischaemic Branch Retinal Vein Occlusion. Ophthalmologica. 2009;223:124-27.
12. Myron Yanoff, Jay S Duker. Ophthalmology, second edition. 2:866-869.
13. Mitry D, Bunce C, Charteris D, Anti-vascular endothelial growth factor for macular edema secondary to branch retinal vein occlusion. Cochrane Database Syst Rev. 2013;1:CD009510. DOI: 10.1002/14651858.CD009510 pub2
14. Smithen LM, Ober MD, Maranan L, Spaide RF. Intravitreal triamcinolone acetonide and intraocular pressure. Am J Ophthalmol. 2004;138.
15. Koyanagi Y, Die Bedeutung der gefasskreuzung fur die entstehung der astthrombose der retinalen zentralvene. Klin Mbl Augenheilk. 1928;81:219-231.
16. Silva RM, Faria de Abreu JR, Cunha-Vaz JG. Blood-retina barrier in acute retinal branch vein occlusion. Graefes Arch Clin Exp Ophthalmol. 1995;233:721–726. [PubMed]
17. Aiello LP, Avery RL, Arrigg PG, Keyt BA, Jampel HD, Shah ST, Pasquale LR, Thieme H, Iwamoto MA, Park JE. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. N Engl J Med. 1994;331:1480–1487. [PubMed]
18. Noma H, Minamoto A, Funatsu H, Tsukamoto H, Nakano K, Yamashita H, Mishima HK. Intravitreal levels of vascular endothelial growth factor and interleukin-6 are correlated with macular edema in branch retinal vein occlusion. Graefes Arch Clin Exp Ophthalmol. 2006;244:309–315.
19. Clarkson JG. Central retinal vein occlusion. In : Ryan SJ, ed: Medical Retina 3RD ed. St.Louis: Mosby Inc. 2001;21:368-1375. Retina.
20. Robert DS, Hiller R, Chew E, Seigel D, Blair N, Thomas CB et al. Risk factors for hemiretinal vein occlusion: Comparison with risk factors for central and branch retinal vein occlusion: The eye disease case control study Ophthalmology. 1998;105(5):765-771.
21. Noma H, Funatsu H, Harino S, Nagaoka T, Yamashita H, Hori S, Pathogenesis of macular edema associated with branch retinal vein occlusion and stratergy for treatment. Nihon Ganka Gakka Zasshi. 2010;114(7):557-91.
22. Ophthalmic Photography: Retinal Photography, Angiography, and Electronic Imaging, 2nd Edition; 576-572.
23. Ashok Garg, Lin JT, Jorge LAlio, Rajvardhan Azad, Jerome Jean Bovet, Bojan Pajic, Cyres KMehat. Mastering the tecniques of LASER applications in ophthalmology.
24. Kreutzer TC, Alge CS, Wolf AH, Kook D, Burger J,Strauss R et al. Intravitreal bevacizumab for the treatment of macular edema secondary to branch retinal vein occlusion. Br J Ophthalmol 2008;92(3):351-5
25. Aiello LP, Avery RL, Arrigg PG, Keyt BA, Jampel HD, Shah ST et al. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. N Eng J Med. 1994;331:1480-1487.
26. Boyd SR, Zachary I, Chakravarthy U. Correlation of increased vascular growth factor with neovascularisation and permeability in ischaemic central retinla vein occlusion. Arch J Ophthalmol. 2002;120:1644-1645.
27. Compochiaro PA. Safety and efficacy of intravitreal Ranibizumab (Lucentis) in patients with macular edema secondary to BRVO: Thr BRAVO study. Paper presented at Retina Congress; 2009. Newyork.
28. Salvatore G, Zeimssen F. Bevacizumab: Off label use in ophthalmology. Indian Journal Ophthal 2007;55(6):417-420.

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