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Prospective study of intravitreal triamcinolone acetonide versus bevacizumab with or without laser for macular edema secondary to retinal vein occlusion

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Abstracts
Objective: To assess difference in visual outcome, macular thickness and need for laser treatment in patients receiving intravitreal triamcinolone acetonide or bevacizumab for macular oedema secondary to retinal vein occlusion.
Design: Open labeled prospective randomised controlled trial, evaluating 38 retinal vein occlusion patients. 19 patients each were assigned, to Intravitreal Triamcinolone Acetonide (IVTA) and Bevacizumab (IVB) group.
Methodology: Baseline ocular parameters like best corrected visual acuity (BCVA), intraocular pressure (IOP) by Applanation tonometry, fundus examination using indirect ophthalmoscope, slit lamp biomicroscopy, Ocular Coherence Tomography of the macula and Fundus Flourescein Angiography performed. Under aseptic conditions, Injection of 4 mg (0.1 ml) Triamcinolone Acetonide (Kenacort) or 1.25 mg (0.05 ml) Bevacizumab (Avastin) was injected into the vitreous. Patients were given re-injections or laser treatment according to requirement. BCVA and IOP at 15 days, 1, 3 and 6 months post injection was recorded. OCT and FFA were repeated at 3 and 6 month.
Outcome: At 6 months, patients with BRVO receiving IVTA, there was significant improvement in visual acuity ($p = 0.014$), as well as decrease in macular edema ($p \approx 0.000$), whereas patients of BRVO in the IVB group did not show significant improvement in visual acuity ($p= 0.375$). Visual acuity of CRVO patients in the IVTA ($p = 0.178$) and IVB ($p = 0.109$) group did not show any significant improvement. Though there was significant decrease in macular edema in both IVTA ($p \approx 0.000$) and IVB ($p =0.042$) groups. No significant increase in IOP was noted in either IVTA ($p= 0.089$) or IVB ($p = o.637$).
Results and Conclusion: The results show a favourable influence of IVTA on BCVA at 6 months.
Positive effect in decreasing central macular thickness (CMT) was observed in patients receiving IVTA and IVB.
FFA guided laser photocoagulation helps in stabilizing the visual acuity and prevents vision threatening complications. Changes in OCT can be used to monitor patient response to treatments for CRVO related macular oedema.
Summary: IVTA injection when combined with FFA guided laser in BRVO eyes showed most favourable outcome in terms of both visual improvement and CMT during follow up period of 6 months.

Keywords: Retinal vein occlusion, macular oedema, FFA, OCT, Intravitreal triamcinolone Acetonide, Intravitreal Bevacizumab, retinal laser

Introduction

Retinal Vein Occlusion is a common cause of vision loss and affects an estimated 16.4 million people around the world. In a large population based study from Israel, the 4 year incidence of retinal vein occlusion for patients aged 40 years or older was 2.14 per 1000. For patients older than 64 years, the 4 year incidence was 5.36 per 1000. Branch Retinal Vein Occlusion (BRVO) accounted for 69.5% of cases [1].

The standard of therapy currently remains limited to the management of the neovascular sequelae with sector peripheral photocoagulation. The Central Vein Occlusion Study showed that the grid pattern photocoagulation definitely reduced macular edema on fluorescein angiography but failed to show statistically significant visual acuity benefit. Recent reports have suggested other treatment modalities investigated in case series, including laser-induced chorioretinal venous anastomosis, intravitreal tissue plasminogen activator [2, 3], surgical induction of chorioretinal venous anastomosis, and radial optic neurotomy [4], to improve the circulatory status of the retina after Central Retinal Vein Occlusion(CRVO).

However, these studies, although encouraging, are still controversial and have not yet been sufficiently supported by larger randomised clinical trials.

Recently, the effect of intravitreal injection of Triamcinolone Acetonide [5-10] and of anti-Vascular Endothelial Growth Factors (anti-VEGF) agents, such as Bevacizumab [13] and Ranibizumab [14], has been widely discussed. They have been reported to be associated with short-term favourable anatomic and functional improvement in some patients with macular edema due to CRVO/BRVO. In view of these promising preliminary results, and considering the fact that there are very few similar studies on Indian population, we performed a prospective study to compare the morphological and visual acuity outcomes associated with intravitreal injection of Triamcinolone Acetonide versus Bevacizumab with or without need for laser in the management of macular edema secondary to BRVO/CRVO. Also, we have included Fundus Fluorescein Angiography as one of the criteria to aid treatment and assess response to treatment.

Aim

To study the visual outcome and macular thickness in patients receiving intravitreal Triamcinolone Acetonide versus Bevacizumab with or without laser for macular edema secondary to retinal vein occlusion.

Objectives

1. To assess difference in macular thickness following intravitreal Triamcinolone Acetonide versus Bevacizumab.
2. To assess difference in visual outcome between these two subgroups.
3. To assess need for laser treatment in both the groups and correlate with macular thickness and visual outcome.

Materials and Methods

The study adhered to the tenets of Declaration of Helsinki. All participants gave written informed consent after going through the patient information sheet. Approval of local ethics committee was obtained. A subject pool of 38 eyes of patient with branch retinal vein occlusion/ central retinal vein occlusion with macular edema, willing to undergo intravitreal injection with or without laser therapy, were studied over a period of 2 years in our institute. 19 eyes received 4mg/0.1ml intravitreal Triamcinolone Acetonide and 19 eyes were given 1.25mg/0.05ml intravitreal Bevacizumab after randomization. Patients who accepted intravitreal Triamcinolone Acetonide constituted the 'IVTA' group and those received intravitreal Bevacizumab constituted the 'IVB' group.

It was a prospective study evaluating visual improvement and intra ocular pressure at 15 days, 1 month, 3 months and 6 months and central macular thickness and leakage on FFA at 3 and 6 months post injection.

Inclusion criteria

1. Age 40-70 years
2. Macular thickness >300 microns on OCT at presentation (untreated).

Exclusion criteri

1. Significant media opacity or inflammation or advanced glaucoma.
2. Pregnant/ lactating females.
3. Patients with renal failure.
4. Patients allergic to fluorescein.
5. Patients with history of Cerebrovascular Accident/ Ischaemic Heart Disease.
6. Patients with pre-existing retinal vascular disease like Diabetic retinopathy, Vasculitis; Age Related Macular Degeneraion.
7. Patients who have previously been treated for vein occlusion.

Method of collection of data

An open label prospective randomized controlled trial was undertaken over a period of 2 years between 1st September 2012 to 28th February 2014. All patients diagnosed as branch retinal vein occlusion/central retinal vein occlusion with macular edema who were willing to participate were included. Minimum sample size in each group was 19 (eyes) patients with branch/ central retinal vein occlusion with macular edema. Sample size was calculated using primer software using α error of 5% and β error of 20%. Considering 80% compliance with a dropout of 5%, a multiplication factor of 1.05 was used to get a sample size of 19 in each group. Patients were randomly allocated into two groups to receive injection IVTA/IVB according to computer generated random numbers using sealed envelope technique. Patient's age, gender, systemic illness, present treatment were noted. Detailed clinical examination of both eyes was done by various methods for diagnosis of branch retinal vein occlusion/ central retinal vein occlusion.

Baseline ocular parameters recorded were

1. Best corrected visual acuity (by Snellens chart), which was converted to logMAR scale.
2. Intraocular pressure (by Goldman Applanation tonometry, model AT 020).
3. Fundus examination using direct ophthalmoscope, indirect ophthalmoscope, slit lamp biomicroscopy with +78D/+90D lenses.
4. Central Macular Thickness (Optical Coherence Tomography, Cirrus, 400)
5. Stereo colour fundus photographs and Fundus Fluorescein Angiography performed with Topcon TRC.50 retinal camera teleconverter TC 201. The photographs included pictures of macula, disc and all quadrants.

FFA grading of the fundus was done considering amount of fluorescein leakage as per ETDRS criteria and patients were allotted points as below [9, 1].

1. No leakage – 0 points
2. Focal- Focal leakage from microaneurysms and dilated capillary segments was awarded 1 point
3. Diffuse – The late diffuse leakage of Fluorescein from unknown source due to generalized breakdown of inner retinal barrier, leading to leakage from retinal capillaries and arterioles was awarded 2 points
4. Combined focal + diffuse leakage – 3 points
5. Cystoid – late staining of the fovea in the petalloid appearance was awarded 4 points.

Materials required for performing the following procedures are as given below:

A. For FFA
- Topcon TRC.50 retinal camera teleconverter TC 201.
- Injection Fluorescein 10% (3ml)
- Scalp vein, syringes (5cc), needles (20G, 26G needle).
- Standby emergency trolley

B. For injection
- Sterile trolley with towels
- Antiseptic solutions- Betadine, Betascrub.
- Syringes (tuberculin syringe)
- Needles (26G)
- Anaesthetic eyedrops (proparacaine hydrochloride 0.5%)
- Drug for injection- Triamcinolone Acetonide 4mg/0.1 ml or Bevacizumab 1.25mg/0.05ml

C. For Laser
- Quantel Medical Vitra, laser class 4, Nd-YAG laser 532nm, 1.2Wmax, Diode laser 650nm, <1mWmax.
- Slit lamp/ Indirect ophthalmoscope.
- Lenses- Volk area centralis fundus/laser lens, Volk Goldmann 3 mirror gonio/fundus lens, Volk QuadrAspheric advanced no fluid lens, Volk Aspheric + 20D lens.

Procedure

All intravitreal injections were performed according to a standard protocol at the Department of Ophthalmology, K. J. Somaiya Hospital. The intravitreal injection of Triamcinolone Acetonide or Bevacizumab was performed under sterile conditions in the ophthalmologic operation theatre with an operating microscope. After obtaining informed consent, adequate pupillary dilatation was achieved, the affected eye was applied with topical application of 5% povidone-iodine for the lids and conjunctiva before the intravitreal injection. Then, the patient was completely draped. An eyelid speculum was used to stabilise the eyelids. Topical proparacaine hydrochloride 0.5% eye drop was used to anaesthetise the eye. The injection of 4mg (0.1 ml) crystalline Triamcinolone Acetonide (Kenacort) or 1.25 mg (0.05 ml) Bevacizumab (Avastin) into the vitreous cavity was performed through the pars plana 3.5 to 4mm posterior to the limbus using a 26-gauge needle. After the procedure, an antibiotic eyedrop (Moxifloxacin) was applied.

Post injection, patients were started on topical antibiotic steroid drops (Milflox DM, Sun Pharma) along with topical non steroidal anti inflammatory drops(Unibrom, Ajanta Pharma)

Ocular parameters noted at follow up visits
1. Best corrected visual acuity by Snellens chart (at 15 days, 1 month, 3 months and 6 months).
2. Intraocular pressure by Applanation tonometry (at 15 days, 1 month, 3 months and 6 months).
3. Fundus Fluorescein Angiography (at 3 months and 6 months).
4. Central Macular Thickness (at 3 months and 6 months).

Statistical analysis

Statistical test like unpaired ‘t’ test (for quantitative data), paired ‘t’ test (for pre and post injection data), chi square test (for qualitative data), ANOVA (Analysis of varianc - to analyze the differences between group means) were used as per distribution of data. P value of <0.05 was considered significant.

Observation and Results

Of the 38 patients, 19 (6 men, 13 women) received IVTA and 19 (12 men, 7 women) received IVB for macular edema secondary to CRVO/BRVO. Of the 19 eyes in the IVTA group, 11 eyes were diagnosed as BRVO and 8 eyes were diagnosed as CRVO. As for the IVB group, 9 were BRVO and 10 were CRVO. The sex distribution was similar in the two groups (P = 0.104) as was the mean patient age (59±8.06 years in IVTA versus 56.11±8.123 in IVB group; P =0.278).

The differences between the two treatment groups with regard to patient age, sex, baseline visual acuity, intraocular pressure, central macular thickness and leakage on fundus fluorescein angiography are summarised in Table 1.

Table 1: The Group of IVTA and IVB

	IVTA Group	IVB Group	P value
Disease distribution (CRVO;BRVO)	8;11	10;9	0.516
Male: Female	6:13	12:7	0.104
Mean age (years ± SD)	59±8.062	56.11±8.123	0.278
Mean BCVA(logMAR)	0.6802±0.27785	0.8256±0.30190	0.131
Mean IOP(mmHg ± SD)	17.37±3.655	16.95±5.307	0.777
Mean central macular thickness (µ ±SD)	453.81±239.717	536.58±273.088	0.328
FFA (amount of leakage)	2.2105±0.71328	2.2105±0.91766	1.000
Number of injections	1.2105±0.41885	1.2632±0.65338	0.769

Outcome Measures

The mean visual acuity at presentation in the BRVO patients receiving IVTA was 0.5039±0.20455 versus 0.6899±0.36736 in the IVB group. Significant improvement in visual acuity was observed in the IVTA group at 1 month (p=0.012), 3 months (p=0.009) and 6 months (p=0.014). No significant difference in visual acuity was observed in IVB group with p=0.829 at 15 days and 1 month, p=0.448 at 3 months and p=0.375 at 6 months. Comparison between the two groups showed significant difference at 15 days (p=0.048), at 1 month (p=0.020) and at 3 months (p=0.042) post injection. Though no significant difference was observed at 6 months post injection (p=0.066). (Tables 2 and3). The mean visual acuity at presentation in the CRVO patients receiving IVTA was 0.9225±0.15101 versus 0.9477±0.16539 in the IVB group. No significant improvement in visual acuity was observed in the IVTA group, [15 days (p=0.178), 1 month (p=0.351), 3 months (p=0.351) and 6 months (p=0.178)] nor in the IVB group with p=0.198 at 15 days, 1 month and at 3 months and p=0.109 at 6 months. Comparison between the two groups also showed no significant difference at 15 days (p=0.958), at 1 month (p=0.822) and at 3 months (p=0.860) or at 6 months (p=0.826) post injection. (Tables 4 and 5)

Table 2: Difference in BCVA(log MAR) in BRVO patients at various intervals. P value was calculated using paired T test.

BCVA (LogMar)	Preinjection	15 days post injection (P value)	1 month post injection (P value)	3 months post injection (P value)	6 months post injection (P value)
IVTA	0.5039±0.20455	0.3666±0.35766 (0.084)	0.3191±0.32351 (0.012)	0.3237±0.31387 (0.009)	0.3465±0.30608 (0.014)
IVB	0.6899±0.36736	0.7038±0.34731 (0.829)	0.7038±0.34731 (0.829)	0.6647±0.38289 (0.448)	0.6400±0.36534 (0.375)

Table 3: Difference in BCVA in BRVO patients between the two groups. P value was calculated using independent sample test.

BCVA(LogMar)	IVTA	IVB	P Value
Preinjection	0.5039±.20455	0.6899±0.36736	0.169
15 days post injection	0.36899±0.35766	0.7038±0.34731	0.048
1 month post injection	0.3191±0.32351	0.7038±0.34731	0.020
3 months post injection	0.3237±0.31387	0.6647±0.38289	0.042
6 months post injection	0.3465±0.30608	0.6400±0.365434	0.066

Table 4: Difference in BCVA (log MAR) in CRVO patients at various intervals. P value was calculated using paired T test.

BCVA (LogMar)	Preinjection	15 days post injection (P value)	1 month post injection (P value)	3 months post injection (P value)	6 months post injection (P value)
IVTA	0.9225±0.15101	0.8849±0.21577 (0.178)	0.9069±0.19028 (0.351)	0.9005±0.18424 (0.351)	0.8849±0.21577 (0.178)
IVB	0.9477±0.16539	0.8778±0.31622 (0198)	0.8778±0.31622 (0.198)	0.8778±0.31622 (0.198)	0.8556±0.31448 (0.109)

Table 5: Difference in BCVA in CRVO patients between the two groups. P value was calculated using independent sample test.

BCVA (LogMar)	IVTA	IVB	P Value
Preinjection	0.9225±0.15101	0.9477±0.16539	0.743
15 days post injection	0.8849±0.21577	0.8778±0.31622	0.958
1 month post injection	0.9069±0.19028	0.8778±0.31622	0.822
3 months post injection	0.9005±0.18424	0.8778±0.31622	0.860
6 months post injection	0.8849±0.21577	0.8556±0.31448	0.826

At 6 months follow up, it was observed that CMT had decreased significantly in both the groups: from 453.89±239.717 µ to 425.42±239.661 µ in the IVTA group (p ≈ 0.000) and from 536.58±273.088 µ to 476.0±325.961µ in the IVB group (p = 0.042). Comparison between the two groups however showed no significant difference (p=0.589). (Tables 6 and 7)

Table 6: P value calculated using paired sample test

CMT(µ)	Preinjection	3 months post injection		6 months post injection	
		CMT	P value	CMT	P Value
IVTA	453.89±239.717	434.84±238.141	≈0.000	425.42±239.661	≈0.000
IVB	536.58±273.088	480.68±316.210	0.043	476.00±325.961	0.042

Table 7: P value calculated using ANOVA test

CMT(µ)	IVTA	IVB	P Value
Preinjection	453.89±239.717	536.58±273.088	0.328
3 months post injection	434.84±238.141	480.68±316.210	0.617
6 months post injection	425.42±239.661	476.00±325.961	0.589

No significant difference in the IOP was observed in either group with the IOP change from 17.37 ±3.655 to 15.26±0.920 in the IVTA group (p=0.089) and from 16.95±5.307 to 15.89±7.731 in the IVB group (p=0.637) at 6 month follow up. Likewise at the final follow-up, there was no significant difference in IOP between both the groups (p=0.754). (Tables 8 and 9)

Table 8: P value calculated using paired sample test.

IOP (mmHg)	Preinjection	15 days post injection (P value)	1 month post injection (P value)	3 months post injection (P value)	6 months post injection (P value)
IVTA	17.37±3.655	17.37±3.833 (1.0)	18.0±3.887 (0.517)	16.32±1.006 (0.391)	15.26±0.920 (0.089)
IVB	16.95±5.307	16.74±7.309 (0.909)	17.37±9.685 (0.866)	16.32±8.226 (0.781)	15.89±7.731 (0.637)

Table 9: P value is calculated using independent sample test.

IOP (mmHg)	IVTA	IVB	P Value
Preinjection	17.37±3.655	16.95±5.307	0.777
15 days post injection	17.37±3.833	16.74±7.309	0.741
1 month post injection	18.0±3.887	17.37±9.685	0.793
3 months post injection	16.32±1.006	16.32±8.226	1.000
6 months post injection	15.26±0.920	15.89±7.731	0.754

The mean leakage on FFA pre IVTA injection was 2.2105±0.71328 pre injection, at 3 months- 1.6316±0.76089 (p≈0.000) and at 6 months- 1.6842±0.67104 (p≈0.000). Whereas in the IVB group the mean leakage was 2.2105±0.91766, 1.7368±0.80568 and 1.7368±0.80568 at pre injection, 3 months and 6 months respectively, with a p value of 0.003 and 0.008 between pre injection and 3 months interval and pre injection and 6 months interval respectively.

No significant difference between the two groups was observed at 3 months. The mean leakage in IVTA group was 1.6316±0.76089 versus 1.7368±0.80568 in IVB group (p=0.681). At 6 months IVTA group mean leakage was 1.6842±0.67104 versus 1.7368±0.80568 in IVB group (p=0.828). (Tables 10 and 11)

Table 10: P value was calculated using paired sample test.

FFA(amount of leakage)	Pre injection	3 months post injection		6 months post injection	
		FFA	P value	FFA	P value
IVTA	2.2105±0.71328	1.6316±0.76089	≈0.000	1.6842±0.67104	≈0.000
IVB	2.2105±0.91766	1.7368±0.80568	0.003	1.7368±0.80568	0.008

Table 11: P value was calculated using independent sample test.

FFA (amount of leakage)	IVTA	IVB	P value
Pre injection	2.2105±0.71328	2.2105±0.91766	1.000
3 months post injection	1.6316±0.76089	1.7368±0.80568	0.681
6 months post injection	1.6842±0.67104	1.7368±0.80568	0.828

4 patients received reinjection of Triamcinolone Acetonide at 1 month in the follow-up period. 3 patients had to be given a reinjection of Bevacizumab (case 4, 5, 8) of which case 5 and 8 received a total of 3 injections at an interval of 1 month each.

In IVTA group, Sector peripheral photocoagulation was performed on 7 patients (cases 10, 11, 13, 17, 18, 20, 22) and focal laser was given to 7 patients (cases 1, 7, 14, 15, 30, 34, 38) during the follow-up periods to prevent neovascular sequelae. Of the 19 eyes in IVB group, laser was required in 14 patients of which 4 patients got focal grid laser (cases 2, 3, 28, 29) and 10 patients required sector peripheral photocoagulation (cases 5, 6, 8, 9, 12, 31, 33, 35, 36, 37). Mean number of laser sittings in IVTA group was 1.37±1.16 versus 1.47±1.26 in IVB group. P value being 0.791(not significant).

Discussion

With changing lifestyle and urbanization, diseases like hypertension and diabetes mellitus have become more common, leading to greater prevalence of vein occlusion.

Our study included 38 patients of CRVO/BRVO who received intravitreal Triamcinolone Acetonide/ Bevacizumab injection and best corrected visual acuity, IOP, central macular thickness and leakage on FFA were assessed.

Approximately 81.5% of patients in our study were above the age of 50 years out of which 61.29% were aged more than 60 years. This is consistent with age group distribution in the SCORE study [13] and also to the fact that risk of vein occlusion increases as age advances [14]. According to the Blue Mountains Eye study [15], the prevalence of retinal vein occlusion for each age-specific participant was 0.7%, younger than 60 years; 1.2%, 60 to 69 years; 2.1%, 70 to 79 years; and 4.6%, 80 years or older.

There was slight but non-significant preponderance of females (52.63%) in our trial as against the SCORE study[13] where there was slight insignificant male preponderance and The Blue Mountains Eye Study [15] which showed no significant sex difference.

More than 80% of patients in our study were long standing hypertensives or were diagnosed hypertensive at presentation. Approximately 36% of them were diabetic. CRVO patients more frequently reported history of diabetes mellitus as compared to BRVO patients.

We also found a higher frequency of BRVO in the superotemporal quadrant compared with other quadrants (60%) and the high frequency of the retinal arteriole found lying anterior to the vein toward the vitreous cavity are consistent with earlier findings from Beaver Dam study and elsewhere [16, 17, 18].

Our study showed significant improvement in visual acuity in the BRVO patients who received IVTA (p= 0.014). However significant improvement was not seen in the BRVO patients who received IVB (p=0.375).

Better results observed in the IVTA group may be explained due to the fact that IVTA inhibits VEGF, Interleukin 6, Interleukin 8 and Platelet Derived Growth Factors. Interferon gamma-induction of vascular permeability is also brought down by Triamcinolone[19]. The mechanism of anti-inflammatoy action is shown to be potentiation of epinephrine, vasoconstriction, stabilization of lysosomal membrane, retardation of macrophage movement, prevention of kinin release, inhibition of lymphocyte and neutrophil function and inhibition of prostaglandin synthesis. On the other hand, Bevacizumab inhibits only VEGF which is only one of the mediators causing macular edema.

Also after intravitreal injection of 4mg Triamcinolone Acetonide, measurable concentrations in vitreous would be expected to last for approximately 3 months (93 +/- 28 days) [20]. However the vitreous half-life of 1.25 mg intravitreal bevacizumab is 4.32 days and concentrations of >10 microg/ml bevacizumab were maintained in the vitreous humor only for 30 days [21]. These two factors may have contributed to no improvement in visual acuity in intravitreal bevacizumab group.

Gokce *et al.* [22] evaluated the comparison of intravitreal Triamcinolone and Bevacizumab in patients with macular edema secondary to branch retinal vein occlusion. There was no difference between groups at the 12th month. IVTA was more efficient than IVB in regard to BCVA improvement in nonischemic BRVO in the early follow-up. IVTA made significant retinal thinning compared to IVB in ischemic BRVO in the early period.

BRAVO evaluated the use of monthly intravitreal

Ranibizumab in eyes with macular edema from BRVO[23] and concluded that there was significant gain in vision and decrease in central macular thickness as compared to the sham group. SCORE study [13] demonstrated that there was no difference in visual acuity in eyes treated with IVTA or grid pattern laser at 12 months in BRVO group but in CRVO group it showed significant improvement with IVTA.

Cheng *et al.* [24] conducted a study on BRVO, which showed that there was significant improvement in visual acuity and decrease in macular edema on OCT examination in both the groups. However therapeutic effects showed no statistically significant difference between these two groups with regard to visual acuity and macular thickness decline. The decrease in macular edema was temporary and patients had to receive reinjections.

The CRVO patients in our study in either IVTA (p=0.178) or IVB (p=0.105) group did not show any significant improvement in visual acuity probably due to the fact that CRVO patients in general have a poor prognosis.

Gokce *et al.* [25] compared the 12 months outcomes achieved using intravitreal IVTA injections with those achieved using intravitreal IVB injections for the treatment of patients with macular edema secondary to CRVO and reported that treatment with intravitreal Triamcinolone Acetonide injections seems to be more effective in improving best-corrected visual acuity during the early post injection period in patients suffering from ischemic CRVO, and in decreasing central macular thickness in patients diagnosed with nonischemic CRVO. However, higher intraocular pressure and development of cataract and glaucoma must be considered in patients with CRVO receiving IVTA injections. Change in OCT may be used to monitor patient response to treatments for CRVO related macular oedema.

CRUISE trial [26] 6 months results showed that when monthly intravitreal IVB was given to CRVO patients, there was a significant improvement in vision and decrease in CMT, with no adverse events.

In RETAIN study [27], patients were treated with IVB depending on OCT findings and scatter laser photocoagulation was applied in patients who required injections in two consecutive months. In this study, patients with BRVO had substantial increase in BCVA. Patients with CRVO also maintained the improved BCVA but the mean foveal thickness was less stable than that seen in patients with BRVO.

A comparative study conducted by Ji Won Lim *et al.* [28] on CRVO patients with poor vision showed that IVTA and IVB were associated with a reduction in macular edema; however, it was noted that in the 12 month follow up period, neither IVTA nor IVB achieved any significant visual acuity improvement. Another study conducted by Wu WC, *et al*. at Taiwan [29] showed that IVTA and IVB can both lead to significant improvement in visual acuity and a resolution of macular edema in patients with CRVO. There was no significant difference in efficacy of two drugs but intravitreal Triamcinolone Acetonide seemed to cause more adverse effects than Bevacizumab.

Yet another study by Tao *et al.* [30] suggested that in view of potential complications of intravitreal Triamcinolone Acetonide in terms of intraocular pressure rise and cataractogenesis, Bevacizumab may be preferred over Triamcinolone Acetonide in non-ischaemic CRVO.

Our study showed significant decrease in CMT in IVTA (p=0.000) and in the IVB (p=0.042) group. Need for repeat injections was recurrence of macular edema. Also requirement for repeat injection was lower in our patients because FFA assisted laser was given to significant number of patients, which acted as adjuvant to intravitreal injection, thus decreasing the need for repeated injection.

The BVOS group [31] evaluated whether grid macular laser photocoagulation improved visual outcome in patients with macular edema secondary to BRVO and concluded that there was significant improvement in the visual acuity in patients treated with grid macular laser photocoagulation as compared to control group.

In our study, no significant rise in intraocular pressure was observed (p=0.089 in IVTA and p=0.637 in IVB group). Nor were any complications like development of cataract, iris neovascularization, endophthalmitis, vitreous haemorrhage or retinal detachment in the six month follow up period.

Park *et al.* [32] who conducted a similar study in Korea concluded that there was raised intraocular pressure in patients receiving Triamcinolone Acetonide injections.

The raise in intraocular pressure could be due to direct physical obstruction of trabecular meshwork with crystalline steroid particles [33, 34] or due to increased accumulation of glycosaminoglycans producing biological oedema [35] or increased production of trabecular meshwork-inducible glucocorticoid response protein which could mechanically obstruct aqueous outflow. It may also result due to corticosteroid induced cytoskeletal changes inhibiting pinocytosis of aqueous humour [36].

The BVOS assessed if peripheral scatter argon laser photocoagulation was useful in preventing the development of neovascularization and vitreous haemorrhage [37], with results in favour of scatter argon laser photocoagulation in preventing the development of neovascularization and vitreous haemorrhage; whereas Shilling and Jones [38] reported improvement in visual acuity after scatter argon laser photocoagulation with areas containing capillary leakage with no encouraging results.

Hayreh *et al.* [39] conducted a study assessing scatter argon laser photocoagulation versus no treatment in the prevention of retinal and/or optic disc neovascularization, and vitreous haemorrhage in BRVO and compared the effects of the two interventions on mean visual acuity, visual field and macular changes. The study reported a beneficial effect of laser treatment for prevention of retinal neovascularization and vitreous haemorrhage, but laser therapy caused a worsening of peripheral visual fields. No effect between groups was observed on visual acuity levels or presence of macular retinal changes.

The CVOS [40] observed that prophylactic panretinal photocoagulation had no significant effect on the development of iris or angle neovascularization. PRP treatment in eyes with established anterior segment neovascularization stimulated its regression and minimizes the risk of development of neovascular glaucoma. CVOS also concluded that grid pattern laser photocoagulation reduced the angiographic CME, but had no beneficial effect on visual acuity as compared with untreated eyes [41].

Fundus photographs and FFA images were evaluated by us at various intervals. It was observed that there was significant decrease in areas of leakage in both the groups (p≈0.00 in IVTA and p=0.008 in IVB group). Also the patients with the decrease in fluorescein leakage were the

ones whose vision had improved significantly. No significant difference among the two groups was observed. Unlike other studies, number of laser sittings was determined by visual improvement and amount of leakage on FFA.

Limitations of our study

1. Study duration was only 6 months. Therefore long term visual outcomes and complications could not be assessed.
2. Study could not be done on a larger population.
3. Hematologic abnormalities have been noted to be associated with RVO. But in our set up we did not investigate the patients for the same hence we cannot comment on it.
4. We have not recorded duration of symptoms, so its correlation with visual improvement could not be assessed.

Summary and conclusion

The results of sample of 38 eyes of 38 patients shows a favourable influence of intravitreal Triamcinolone Acetonide on best corrected visual acuity (p= 0.014) at 6 months.

Branch retinal vein occlusion patients receiving intravitreal Bevacizumab did not show improvement in terms of best corrected visual acuity (p=0.375 at 6 months).

Central retinal vein occlusion patients in general did not show improvement in best corrected visual acuity (p=0.178 in IVTA and p=0.109 in IVB group) probably due to the fact that basic prognosis of central retinal vein occlusion is poor. Positive effect in decreasing central macular thickness was observed in patients receiving IVTA (p≈0.000) and IVB (p=0.042).

FFA guided laser photocoagulation helps in stabilizing the visual acuity and prevents vision threatening complications due to less need for injections. Changes in OCT can be used to monitor patient response to treatments for CRVO related macular oedema.

To summarise, IVTA injection when combined with FFA guided laser in BRVO eyes showed most favourable outcome in terms of both visual improvement and CMT during follow up period of 6 months.

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