Efficacy of Intravitreal Triamcinolone Acetonide in the Early Treatment of Macular Oedema Due to Retinal Vein Occlusion

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Macular oedema occurs in a wide variety of ocular diseases. It is a common cause of vision deprivation in retinal vein occlusion. It may occur in central retinal vein occlusion (CRVO) or in branch retinal vein occlusion (BRVO). Now a days, the potential use of intravitreal Triamcinolone acetonide is being trailed for relieving macular oedema in CRVO and BRVO. Early treatment of macular oedema with IVTA is necessary as longstanding macular oedema results in irreversible photoreceptor damage. This prospective case control study was carried out at department of Ophthalmology, Dinajpur Medical College Hospital, Dinajpur from January 2012 to July 2015. A comparative study of changes in visual outcome and status of macular oedema was conducted between two groups of patients. One group observed after intravitreal injection of Triamcinolone acetonide and the other group without injection. 30 patients were randomly selected for IVTA group and another 30 patients for the control group. 4 mg/0.1ml preservative free TA was used. Patients were followed up at two wks, one month and three months after TA injection. Mean age distrubution in IVTA group was 61± 10.65 and in the control group 60± 10.84. Mean V/A in IVTA group was 0.80± 0.37 (SD) and 1.06± 0.25(SD) in the control group after 01 month of injection. Mean V/A in IVTA group was 0.70± 0.29 (SD) and 1.05± 0.26 (SD) in the control group after 03 months of injection. In the IVTA group macular oedema was present in 14 (46.67%) cases and absent in 16 (53.33%) cases after 1 month of injection. In the control group 22 (73.33%) cases had macular oedema and macular oedema was absent in only 08 (26.67%) cases. In the IVTA group macular oedema was present in 10 (33.33%) cases and absent in 20 (66.67%) cases after 3 months of injection. In the control group 18 (60%) cases had macular oedema and macular oedema was absent in 12 (40%) cases after 3 months. From this prospective, randomized case-control study it was evident that early treatment of retinal vein occlusion cases (CRVO or BRVO) with intravitreal Triamcinolone acetonide is significantly effective in the treatment of macular oedema due to venous occlusions.

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Introduction

Macular oedema occurs in a wide variety of ocular diseases. It is a common cause of vision deprivation in retinal vein occlusion. It may occur in central retinal vein occlusion (CRVO) or in branch retinal vein occlusion (BRVO).

The basic mechanisms involved in both types of retinal vein occlusions are:

- External compression of the vein ,
- Venous stasis and,
- Degenerative diseases of the venous endothelium.

It was noted that visual acuity gain was decreased with duration of occlusion. This may be due to irreversible damage of photoreceptor cells by the oedema as demonstrated in histopathological studies.[1]

Now a days, the potential use of intravitreal Triamcinolone acetonide is being trailed for relieving macular oedema in CRVO and BRVO. Triamcinolone acetonide is a relatively insoluble long acting steroid that has been used for decades in the treatment of ocular inflammations by peribulbar or subtenon's injection and now its use via intravitreal route has also shown encouraging results. The duration of visible crystalline intravitreal Triamcinolone acetonide is about two months, presumably giving an extended period of time for its action to occur in tissues adjacent to the vitreous cavity. IVTA appeared to be well tolerated, with a favourable effect on the course of the disease over an 18 months period.[2]

Yepremyan *et al* [3] conducted a study in Boston, USA on the effect of IVTA for the early treatment of macular oedema in BRVO patients and found many potential benefits including prompt resolution of macular oedema resulting in a dramatic early improvement in visual acuity. In another study, Greenberg *et al* [4] showed that CRVO with macular oedema had significant improvement in visual acuity and complete resolution of macular oedema after injection of IVTA. IVTA appears to be effective in reducing cystoid macular oedema associated with CRVO. This reduction often corresponded to an improvement in visual acuity.[5] Michael Ip *et al* [6] found no adverse effects like cataract, glaucoma, retinal detachment or endophthalmitis, after injecting IVTA. IVTA may be a safe and effective treatment in the macular oedema due to CRVO.[7]

Early treatment of macular oedema with IVTA is necessary as longstanding macular oedema results in irreversible photoreceptor damage. The mechanism by which IVTA works is unclear, though stabilization of the blood retinal barrier may play a significant part.[8]

This study was designed to observe the efficacy of IVTA for the early resolution of macular oedema caused by retinal vein occlusions (CRVO & BRVO).

Methods

A comparative study of changes in visual outcome and status of macular oedema was conducted between two groups of patients. One group observed after intravitreal injection of Triamcinolone acetonide and the other group without injection.

Type of the study: Prospective case control study.

Period of the study: January 2012 to july 2015

Place of the study: Department of Ophthalmology, Dinajpur Medical College Hospital, Dinajpur.

Inclusion criteria: Patients of recent CRVO and BRVO with macular oedema and visual acuity of equal or less than 6/24.

Exclusion criteria:

- Macular oedema due to causes other than retinal vein occlusions.
- Old cases with signs of neovascularizations or when clear FFA picture is possible.
- Raised IOP.

Grouping and randomization**:** In this study, CRVO and BRVO patients were randomly selected by lottery method for two groups. One group receiving a single dose (4 mg) of intravitreal Triamcinolone acetonide immediately after diagnosis (IVTA group) and the other group not receiving injection (Control group) receiving conventional treatment protocol. Both groups were followed up for a period of 3 months.

Sample size: 30 patients were randomly selected for IVTA group and another 30 patients for the control group.
All patients underwent through ocular examination and systemic evaluation to find out the cause and risk factors. Through investigations done and specific investigations done where necessary.

Evaluation of Macular oedema: Macular oedema was measured in terms of either present or absent by slit lamp biomicroscopy with 78 D volk lens as follows-
Macular oedema present : Presence of macular thickening and /or hard exudates in macula.

Macular oedema absent: Absence of macular thickening and /or hard exudates in macula.
Fundus fluorescein angiography were done in selected cases.

IVTA given maintaining standard aseptic protocol. 4 mg/0.1ml preservative free TA was used. Patients were followed up at two wks, one month and three months after TA injection.

Statistical Analysis
Data were collected in a pre-designed data collection sheet and then compiled accordingly. Appropriate statistical analysis was done using computer based software SPSS program. Status of visual acuity, macular oedema, intraocular pressure were measured and compared between the two groups. Unpaired 't' test was done to determine the difference of visual acuity between two groups. Chi-sqaure test was used for evaluating change of macular oedema and 't' unpaired test for change of IOP between two groups. A probability 'p' of equal or less than 0.05 was considered significant and 'p' value > 0.05 was considered nonsignificant.

Results
The results are shown in tabulated form below -

Table I**:** Age distribution in IVTA group (n=30) and Control group (n = 30)

Age in year	IVTA group (n=30)		Control group (n = 30)		p value
	No. of cases	%	No. of cases	%	
40 - 65	20	66.67	21	70	> 0.50 ns
66 - 90	10	33.33	09	30	

Mean age distribution in IVTA group was 61 ± 10.65 and in the control group 60 ± 10.84

Table II: Sex distribution in IVTA group (n = 30) and Control group (n = 30)

Sex	IVTA group (n = 30)		Control group (n = 30)		p value
	No. of cases	%	No. of cases	%	
Male	12	40	14	46.67	>0.50 ns
Female	18	60	16	53.33	

Table III: Distribution of aetiologic factors in IVTA group (n = 30) and Control group (n = 30)

Aetiologic factors	IVTA group (n=30)		Control group (n = 30)	
	No. of cases	%	No. of cases	%
Diabetes	6	20	5	16.67
Hypertension	12	40	10	33.33
Hyperlipidaemia	9	30	10	33.33
Others	3	10	5	16.67

Table IV: Distribution of type of retinal vein occlusions in IVTA group (n = 30) and Control group (n = 30)

Type of occlusions		IVTA group (n=30)		Control group (n = 30)	
		No. of cases	%	No. of cases	%
CRVO		06	20	05	16.67
BRVO	Major	16	53.33	18	60
	Minor	08	26.67	07	23.33

Table V: Distribution of baseline visual acuity in IVTA group (n = 30) and Control group (n = 30)

Visual acuity	IVTA group (n = 30)			Control group (n = 30)			P
	No. of cases	%	Mean V/A (log MAR equivalent) ± SD	No. of cases	%	Mean V/A (log MAR equivalent) ± SD	
6 / 24	02	6.67	1.18 ± 0.475	03	10	1.16 ± 0.484	>0.05
6/36	04	13.33		04	13.33		
6/60	10	33.33		08	26.67		
< 6/60	14	46.67		15	50		

Baseline mean V/A converted in log MAR equivalent in IVTA group was 1.18 ± 0.475 (SD) and in the control group was 1.16 ± 0.484 (SD). 't' unpaired test was done.

Table VI**:** Distribution of V/A after 1 month in IVTA group (n = 30) and Control group (n = 30)

V/A	IVTA group (n = 30)			Control group (n = 30)			P value
	No. of cases	%	Mean V/A (log MAR equivalent) ± SD	No. of cases	%	Mean V/A (log MAR equivalent) ± SD	
6 / 9	01	3.33	0.80 ± 0.37	00	00	1.06 ± 0.25	<0.01**
6/12	03	10		00	00		
6/18	04	13.33		00	00		
6/24	05	16.67		02	6.67		
6/36	06	20		03	10		
6/60	05	16.67		12	40		
< 6/60	06	20		13	43.33		

Mean V/A in IVTA group was 0.80 ± 0.37 (SD) and 1.06 ± 0.25(SD) in the control group after 1 month. 't' unpaired test was done. ** = Significant ($p < 0.01$).

Table VII**:** Distribution of V/A after 3 months in IVTA group (n = 30) and Control group (n = 30)

V/A	IVTA group (n = 30)			Control group (n = 30)			P value
	No. of cases	%	Mean V/A (log MAR equivalent) ± SD	No. of cases	%	Mean V/A (log MAR equivalent) ± SD	
6 / 9	01	3.33	0.70 ± 0.29	00	00	1.05 ± 0.26	< 0.01***
6/12	04	13.33		00	00		
6/18	05	16.67		01	3.33		
6/24	06	20		02	6.67		
6/36	06	20		02	6.67		
6/60	05	16.67		12	40		
< 6/60	03	10		13	43.33		

Mean V/A in IVTA group was 0.70 ± 0.29 (SD) and 1.05 ± 0.26 (SD) in the control group after 3 months. 't' unpaired test was done. . *** = Highly significant ($p < 0.01$).

Table VIII: Distribution of macular oedema after 1 month in the IVTA group (n = 30) and Control group (n = 30)

Macular oedema	IVTA group (n = 30)		Control group (n = 30)		p value
	No. of cases	%	No. of cases	%	
Macular oedema present	14	46.67	22	73.33	< 0.05*
Macular oedema absent	16	53.33	08	26.67	

Chi square (x^2) test was done. . * = Significant ($p < 0.05$).

Table IX: Distribution of macular oedema after 3 months in the IVTA group (n = 30) and Control group (n = 30)

Macular oedema	IVTA group (n = 30)		Control group (n = 30)		p value
	No. of cases	%	No. of cases	%	
Macular oedema present	10	33.33	18	60	
Macular oedema absent	20	66.67	12	40	< 0.05*

Chi square (x^2) test was done. . * = Significant ($p < 0.05$).

Discussion

Macular oedema is the main cause of the poor visual prognosis in retinal vein occlusions. It was noted that visual acuity gain was decreased with duration of occlusion. This may be due to irreversible and permanent damage of photoreceptor cells by the oedema as demonstrated in histopathological studies[1]. Laser treatment was initiated at least three months after the visual insult because in many cases the macular oedema resolves spontaneously, obviating the need for any intervention. The visual prognosis after grid laser in macular oedema is not improved though the oedema get relieved.

The mainstay treatment in CRVO is by panretinal photocoagulation (PRP) to prevent or treat neovascularisation. Laatikainen *et al* [9] in a randomised trial determined that prophylactic xenon panretinal photocoagulation reduced the incidence of neovascularization and macular oedema but had no effect on visual acuity. More recently, however, the CRVO study group recommended providing frequent follow up of at risk patients and application of laser when neovascularization occurs (The Central Vein Occlusion study group, 1995) because there was no benefit of prophylactic therapy over therapy when complications arise. Hayreh *et al* [10] found no benefit from laser photocoagulation in CRVO, stating that photocoagulation has a detrimental effect on visual field.

Now-a-days, the potential use of intravitreal Triamcinolone acetonide is being trailed for relieving macular oedema in CRVO and BRVO. Triamcinolone acentonide is a relatively insoluble long acting steroid that has been used for decades in the treatment of ocular inflammations by peribulbar or sbutenon's injection and now its use via intravitreal route has also shown encouraging results. The duration of visible intravitreal crystalline Triamcinolone acetonide (TA) is about 2 months, presumably giving an extended period of time for its actions to occur in tissues adjacent to the vitreous cavity. Intravitreal TA appeared to be well tolerated, with a

favourable effect on the course of the disease over an 18 months period. Yepremyan et al [3] conducted a study in Boston, USA on the effect of IVTA for the early treatment of macular oedema in BRVO patients and found many potential benefits including prompt resolution of macular oedema resulting in a dramatic early improvement in visual acuity. In another study, Greenberg *et al* [4] showed that CRVO with macular oedema had significant improvement in visual acuity and complete resolution of macular oedema after injection of IVTA. IVTA appears to be effective in reducing cystoid macular oedema associated with CRVO. This reduction often corresponded to an improvement in visual acuity. Michael Ip *et al* [7] found no adverse effects like cataract, glaucoma, retinal detachment or endophthalmitis after injecting IVTA and concluded that IVTA may be a safe and effective treatment in the macular oedema due to CRVO. Early treatment of macular oedema with IVTA is necessary as longstanding macular oedema results in irreversible photoreceptor damage. The mechanism by which IVTA works in unclear though stabilization of the blood retinal barrier may play a significant part.

This study was conducted on the patients of retinal vein occlusions either CRVO or BRVO attending the Dept. of Opthalmology, DjMCH, Dinajpur to observe the effect of intravitreal Triamcinolone acentonide (IVTA) in the treatment of macular oedema. Conventional principle of management of retinal venous occlusions of recent onset is primarily aimed at the investigation and management of the predisposing factor and observation of the case for 3-4 months so that fundal haemorrhages and exudates are cleared off and then FFA is carried out to initiate the specific treatment. From this ground, the patients of retinal venous occlusions were randomly grouped into two. One group (IVTA group) recived early treatment with a single dose of 4 mg (0.1 ml) intravitreal Triamcinolone acetonide injection and the other group (Conrol group) were observed with some traditional treatment like topical NSAIDs, low dose aspirin, IOP lowering agents, etc.

In this study maximum patients were in the age group, 40 - 65 years, 20 (66.67%) cases in IVTA group and 21 cases (70%) in the control group. It was seen that among the total 60 cases the majority 22 (36.67%) cases had hypertension as the aetiologic factor.

Snellen Visual acuity chart was utillized for the measurement of visual recording. Highest base-line V/A recorded was 6/24-2 in IVTA group and 3 in control group. After 3 months of IVTA injection one achieved V/A 6/9 and the other V/A 6/12. But one had achieved V/A of 6/18 out of 30 cases of control grop. The lowest V/A recorded was HM (hand movement) from 2 feet 01 in IVTA group. After 3 months of IVTA injection it achieved V/A of 6/600 (Counting finger from 2 feet). It was an ischaemic CRVO case. V/A < 6/60 in IVTA group was 14 (46.67%) which was reduced to 03 (10%) after 3 months. Whereas in the control group V/A<6/60 was in 15 (50%) which was changed to 13 (43.33%) after 3 months.

Improvement of mean V/A after 1 month in IVTA group was 0.38 and after 3 months 0.48. On the other hand, improvement of mean V/A in control group after 1 month was 0.10 and after 3 months 0.11. For statistical purpose to see the improvement of vision, logMAR equivalent of Snellen acuity was used after Jonas *et al* [11] of Germany. According to Jonas *et al* [11] best achieved V/A after injection was 0.45 $\pm$ 0.27. In this study best achieved mean visual acuity was 0.70 $\pm$ 29. No gain of visual acuity found in IVTA group was 02 (6.67%) and 09 (30%) in the control group. These results are consistent with those of Jonas *et al* [11], Ip MS *et al* [7] and Rakie *et al.*[12] Zhang *et al* [13] of Beijing University has shown in 2002 that there is a close

relationship between intital V/A and visual prognosis. He has shown that the mean V/A was 0.40 in CRVO, 0.50 in HRVO and 0.58 in BRVO. This study also has found that final V/A is better in BRVO cases than CRVO and non-ischaemic cases than ischaemic cases. As has shown by Meher yepremyan, this study also shows that intravitreal Triamcinolone acetonide initiates quicker recovery of vision which is very important for a person to return to his day to day activities as early as possible.

For the assessment of macular oedema, clinical judgment by slit-lamp biomicroscopy with 78 D volk lens and angiographic evidences were taken into account. In the IVTA group, macular oedema was present in 10 (33.33%) cases and absent in 20 (66.67%) cases after 3 months of injection. On the other hand, in the control group, 18 (60%) cases had macular oedema and macular oedema was absent in 12 (40%) cases after 3 months.
In the follow up there was no evidences of cataract, endophthalmitis or retinal break and RD.

Conclusion

From this prospective, randomized case-control study it was eveident that early treatment of retinal vein occlusion cases (CRVO or BRVO) with intravitreal Triamcinolone acetonide is significantly effective in the treatment of macular oedema due to venous occlusions.

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