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EFFICACY OF INTRAVITREAL RANIBIZUMAB AND LASER PHOTOCOAGULATION IN THE TREATMENT OF DIABETIC MACULAR EDEMA

Ophthalmology

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ABSTRACT

Objective: To study the efficacy of intravitreal Ranibizumab and laser photocoagulation in the treatment of diabetic macular edema and to compare the two treatment arms.

Design: prospective, randomized, interventional, hospital-based study.

Material and methods: 40 eyes of 40 patients with diabetic macular edema(DME), attending the outpatient department of department of ophthalmology, SRMS-IMS,Bareilly, UPwere enrolled in the study. Patients were randomized into two groups, A and B, baseline evaluation was done, including optical coherence tomography (OCT) and fundus fluorescein angiography (FFA).Intravitreal ranibizumab was given to the patients in group A while laser photocoagulation was administered in group B.

Results: At 2 months follow up there was significant ($p<0.05$) improvement in the q best corrected visual acuity (BCVA) and central macular thickness (CMT) in both the treatment groups.no serious adverse effects were seen.

Conclusion: Both laser photocoagulation and intravitreal ranibizumab prove to be safe and effective method in management of DME.

KEYWORDS

INTRODUCTION:

Diabetic retinopathy is a leading cause of visual impairment worldwideand diabetic macular edema (DME) is the most common cause of vision loss in these patients.[1] DME results from breakdown of the vascular inner blood-retinal barrier (BRB). It may be focal or diffuseand can occur in two ways[2]: (1) focal leakage arising from microaneurysms; and (2) diffuse leaking arising from the wall of capillaries.

Control of blood glucose level and blood pressure has been shown to slow the progression of diabetic eye disease.[3]However, in many patients, even after a good diabetic control, if left untreated DME can result in significant vision loss.[4] It is also evident that progression of DME is associated with duration of disease, poor glycemic control andthe need for insulin[5]in type 2 diabetes.

Periodic fundus examinations are recommended by Early Treatment Diabetic Retinopathy Study (ETDRS).Majority of diabetic individuals, who lose vision, is not because of an inability to treat the disease, but rather due to a delay in seeking medical attention.[6]Thus, dilated fundus examination by direct and indirect ophthalmoscopy should be done to detect diabetic changes and any macular edema that might require intervention. OCT is a non-contact and non-invasive tool,[7,8] that enables precise measurement of macular thickness. Thus, it facilitates early detection of macular edema and also helps in monitoring the therapy. FFA is another important tool to assess the functional integrity of retinal vasculature.

A number of treatment trials have been done and many are still ongoing. In order to achieve a stable, dry macula with minimal adverse effect, laser therapy, intravitreal steroids and intravitreal anti-VEGF form the main stay of treatment.

We conducted this study to assess whether there was a significant difference between intravitreal ranibizumab and laser photocoagulation as a single primary treatment of DME, by evaluating the BCVA and CMT on OCT at 2 months.

MATERIALAND METHODS:

This was a prospective, randomized, interventional hospital-based study done in the department of ophthalmology, SRMS-IMS, Bareilly, UP between August'18 to june'19.

40 eyes of 40 patients, with diabetic macular edema, who fulfilled the inclusion criteria, were enrolled. Patients were allocated into two groups, group A (intravitreal ranibizumab group) and group B (laser group) by block randomization.

INCLUSION CRITERIA:

Study groups included both male and female patients, with age ≥ 18 years, having either type 1 or 2 diabetes, HbA1C >6% and with visual impairment due to diabetic macular edema (DME).

EXCLUSION CRITERIA

Exclusion criteria were: (i) Presence of any concomitant condition in the study eye like CRVO, BRVO etc., likely to cause macular edema or decrease in visual acuity (ii) History of previous treatment for DME (iii) Opaque media like dense cataract and vitreous hemorrhage (iv) History of stroke (v) Uncontrolled glaucoma in either eye (vi) HbA1C >10% Study was approved by hospital ethical committee. A written informed consent and detailed history was taken from all the patients.

Complete ophthalmic examination which included UCVA and BCVA by Snellen visual acuity chart, detailed slit lamp examination, direct and indirect fundus examination,intraocular pressure by applanation tonometry, was done.

Fundus fluorescein angiography (FFA)was performed at base line and Optical Coherence Tomography (OCT)was performed at day 1 (baseline), at 2-week and at 2-month to evaluate the macular edema and monitor the response of therapy.

TREATMENT:

After initial evaluation, patients in group A were given intravitreal Ranibizumab (0.5mg), under full aseptic conditions while patients in group B were subjected to laser photocoagulation. Follow up was done at 2-week and at 2-month, post procedure. Visual acuity and central macular thickness (using OCT) was assessed at each follow-up visits, as outcome measures.

OBSERVATIONS AND RESULTS

Demographic data:

A total of 40 eyes of 40 patients were enrolled in the study.20 patients were assigned for laser group and 20 or intravitreal ranibizumab group. Mean age, sex distribution, duration of Diabetes Mellitus (DM), status of HbA1C baseline visual acuity, and baseline central macular thickness (CMT) of patients in the group A and B are shown in the table 1.

Table 1: baseline characteristics in both the study groups

		GROUP A N (%)	GROUP B N (%)	p value (Independent T test)
AGE (years)	mean	52.52	53.11	p=0.835
GENDER	Male	9 (45)	8 (40)	P = 1
	Female	11 (55)	12 (60)	P = 1
mean HbA1C (%)		8.6	8.4	P > 0.05
Mean duration of diabetes (years)		8.8	9	P > 0.05
Baseline BCVA (log MAR units)	mean	1.02	1.16	p = 0.091
Baseline CMT (microns)	mean	368	371	P = 0.894

Hence, no statistically significant differences were observed regardingbaseline parameters between the two groups.

Table 2: Distribution of cases according to severity of DME

Severity of DME	Group A (n = 20)		Group B (n = 20)	
	N	%	N	%
Mild	8	40	7	35
Moderate	10	50	12	60
Severe	2	10	1	5

Based on international clinical diabetic macular edema disease severity scale, most of the patients in our study belongs to mild to moderate DME and the distribution in the two groups was comparable (p = 0.748)

Table 3: comparison of BCVA within each group at baseline, at 2-week, and at 2-month

	Baseline	2-week	2-month	P value
Group A	1.02	0.7044	0.5140	P < 0.05
Group B	1.16	0.769	0.5857	P < 0.05

Thus, there was significant improvement (p< 0.05) in the BCVA in each group at 2-month

Table 4: comparison of CMT within each group at baseline, at 2 weeks, and at 2 months

	Baseline	2-week	2-month	P value
Group A	368	281.25	218.50	P<0.05
Group B	371	303	231.25	P<0.05

There was significant (p< 0.05) reduction in the central macular thickness in the two groups.

Table 5: comparison of BCVA between group A and B at baseline and at 2 months

	Group A	Group B	P value
Baseline	1.02	1.16	P>0.05
2-month	0.5140	0.5857	P>0.05

Table 6: comparison of CMT between group A and B at baseline and at 2 months

	Group A	Group B	P value
Baseline	368	371	P > 0.05
2-month	218.5	231.25	P > 0.05

When the change in BCVA and CMT between the two groups was compared, Group A (intravitreal Ranibizumab) had better outcome than group B (Laser group), but the difference was not statistically significant (p > 0.05).

Table 7: mean change in IOP during the study period in the two groups.

	Mean baseline IOP (mmHg)	Mean IOP at 2-month (mmHg)	Mean change in IOP	SD	P value
Group A	15.00	16.25	1.25	0.92	0.21
Group B	14.75	15.75	1.00	0.75	0.13

There was no significant rise in IOP in either of the two groups.

DISCUSSION:

In this study, duration of diabetes and glycemic control (HbA1C) in both the groups were comparable (p > 0.05). Our patients, however, had poor control of DM compared to study by Batioglu and colleagues where HbA1Cwas 4% to 6%.[9]

In our study, intravitreal Ranibizumab and laser were given for the management of DME, and BCVA and CMT were assessed at 2-week and at 2-month, as outcome measures. Two months follow up was chosen as only a single treatment was given. Any retreatment if required was given after 2 months.

The significant improvement in BCVA in intravitreal ranibizumab group (p< 0.05) was in accordance to various clinical trials, including DRCR.net protocol I[10,11], RIDE and RISE[12,13], READ 2[14,15], RESOLVE[16], RESTORE[17], and REVEAL[18]. Since 1985, the mainstay of treatment for clinically significant DME had been focal/grid laser photocoagulation based on the Early Treatment Diabetic Retinopathy Study (ETDRS).[4] Our study also showed significant improvement of BCVA post laser therapy at 2 months (p< 0.05), however a study done by Lee et al[19] showed no significant improvement of BCVA at three months post laser.

Our study also had significant improvement in mean CMT at 2 months in both injection group and laser group, though the outcome was better in intravitreal ranibizumab group, but the difference was not statistically significant (p> 0.05).

The results from the RESTORE study demonstrates that treatment with ranibizumab as monotherapy and combined with laser treatment is superior to laser treatment in rapidly improving and sustaining VA in patients with visual impairments due to DME.[17] The reason for this difference could be short duration of our study (2 months, compared to 12 months in RESTORE study) and small sample size (40 patients compared to 345 patients in RESTORE group).

Though time and again Ranibizumab have proven to be a successful treatment modality for visually significant DME, yet there are certain constrains for its use in developing country like ours. High cost and need for repeated injections are a major cause of loss to follow up or treatment denial.

Although in patients with media opacity such as vitreous hemorrhage, it is not always possible to administer complete laser still certain dreadful adverse effects of Ranibizumab (and other anti-VEGF agents) like endophthalmitis warrants its frequent use. History of stroke is a high-risk factor for intravitreal ranibizumab injection, which is a common occurrence in diabetic and hypertensive patients. The pooled analysis of the 2 pivotal studies, RESOLVE[16] and RESTORE[17], resulted in an incidence rate of 1.4% for endophthalmitis in 1-year study. In our study no adverse effects were seen, which can be attributed to small sample size.

In view of our study, we can say, both the modalities have comparable outcome at two months follow up. Treatment decision has to be individualized according to the patient profile. So, both the treatment should be kept at par. However long term follow up is required to assess the stability of treatment.

CONCLUSION

Both intravitreal ranibizumab and laser photocoagulation showed good comparable outcomes in term of BCVA and macular thickness at two months post treatment as primary treatment for DME.

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