Original Article

Effect of Intravitreal Injection of Bevacizumab with Laser Photocoagulation versus Combination of Intravitreal Injection of Bevacizumab with Triamcinolone Acetonide in the Treatment of Diabetic Macular Edema

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Abstract

Background & Objective: Recently there are various treatment modalities for the patients of diabetic macular edema. So, it is very difficult to choose the option. This study was aimed to compare the efficacy of combination of intravitreal injection of bevacizumab with laser photocoagulation versus combination of intravitreal injection of bevacizumab with triamcinolone acetonide in the treatment of DME.

Methods & Materials: A prospective observational study was conducted on 50 eyes of fifty patients who were diagnosed with DME at vitreo-retina department of NIO&H. They were divided into 2 groups, Group A (treated with bevacizumab with laser photocoagulation) and Group B (treated with intra-vitreal bevacizumab with triamcinolone acetonide). Follow-up pattern was set after 1 and 3 months of intervention. All the baseline data and outcome data were recorded in a pre-designed data collection sheet and was statistically analyzed by SPSS version 23.

Result: Mean baseline BCVA was 0.57±0.29 (SD) Log MAR in group A and 0.70±0.26 (SD) Log MAR in group B (p=0.57). BCVA was 0.40±0.32 (SD) and 0.40±0.37 (SD) in group A and 0.58±0.28 (SD) and 0.45±0.36 (SD) in group B during 1st and 2nd follow-up respectively. Comparison of mean BCVA between two groups at final follow-up was not significant. Improvement of CMT from baseline in every follow up in each group was significant but comparison of mean CMT between two groups at final follow-up was not significant (p=0.64). Though the difference of baseline IOP of both groups are statistically significant, comparison of mean IOP between two groups at final follow-up was not significant (p=0.67).

Conclusion: There was significant improvement in mean BCVA and mean CMT within the group in each follow-up. At final follow-up, Combination of intravitreal bevacizumab and triamcinolone acetonide shows better improvement which is non-significant.

Key words: Diabetic macular edema, Bevacizumab, Triamcinolone Acetonide.

Introduction

Diabetic retinopathy (DR) is an important cause of acquired visual loss and impairment in working age group worldwide. Diabetic macular edema (DME) is a manifestation of diabetic retinopathy that produces loss of central vision.[1]

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Among the diabetic population, the prevalence of DME varies with the affecting rate of 14.3% and 5.6% in type 1 and type 2 diabetic patients, respectively. Duration of diabetes is also a risk factor. Patients living with diabetes for less than 10 years affected less (3.2%) compared with of those having diabetes for more than 20 years (20%). The prevalence of DME is also higher among those with poorer HbA_1C, hypertension and serum cholesterol > 4.0 mmol/l.[2]

The pathophysiology of DME is multifactorial and complex. Although disrupted blood retinal barrier plays a pivotal role in the pathogenesis of DME, accumulation of leucocytes in the non-photocoagulated posterior pole and up-regulation of angiogenic growth factors, such as vascular endothelial growth factor (VEGF) also contribute significantly to the progression of DME.[4]

In the early treatment of DME, focal photocoagulation of eyes with clinically significant macular edema reduced the risk of moderate visual loss by approximately 50%. In spite of treatment, 12% of treated eyes developed moderate visual loss.[3]Also, the treated eyes showed a high rate of recurrence or persistence of macular edema despite appropriate macular laser therapy. Furthermore, laser procedure can be performed as outpatient department (OPD) basis though it is relatively costly.

Recently, newer treatment modalities, such as intravitreal injection of biological response modifiers that block VEGF, have been developed to increase the efficacy of controlling diabetic macular edema and achieving better visual prognosis. Intravitreal bevacizumab has been effective in cases with center involved DME by improving the visual acuity, reducing macular edema, fibro vascular proliferation in retinal NV and resolution of vitreous hemorrhage. But combination ofintravitreal triamcinolone acetonide (corticosteroid) with intravitreal bevacizumab (IVB) has superior efficacy than IVB alone.[8,9]

Furthermore, imaging advances of DME is facilitated by multiple imaging techniques. Optical coherence tomography (OCT) and fluorescein angiography (FA) can help to predict prognosis and monitoring response to therapy.[10]

Thus, the purpose of this study is to evaluate the efficacy and safety of the combined effect of triamcinolone acetonide and bevacizumab in comparison to Avastin and laser photocoagulation byusing an interventional case series design and to evaluate the visual prognosis and anatomic alterations of macular edema using spectral domain OCT. The current study findings may enrich the existing data hence helps the vitreo-retina specialist as well as policy makers to formulate a guideline for the proper management of DME patients.

Materials and Methods

This prospective observational study was conducted in the department of vitreo-retina, NIO & Hover a period of one and half years from September 2017 to February 2019.50eyes of fifty diagnosed patients of diabetic macular edema attending in the vitreo- retina OPD of NIO&H. having CMT $\geq$ 275 μm by OCT and with controlled blood sugar were included in this study.patients were selected purposively based on specific selection criteria. They were divided into 2 groups, Group A (treated with bevacizumab with laser photocoagulation) and Group B (treated with intra-vitreal bevacizumab with triamcinolone acetonide).

An informed consent was obtained prior to the injection after they had been informed about the benefit, risks, and possible complications of the intervention.Patients of group A were received intravitreal 1.25mg/0.05ml bevacizumab was injected through the inferotemporal pars plana 4 mm away from the limbus in phakic eye and 3.5mm away in pseudophakic or aphakic eye directed towards the center of the vitreous followed by laser from slit lamp delivery system of NIDEK diode posterior laser machine. Only one session of laser was given to each patient in laser group. Laser was given by vitreo-retina specialist.

Patients of group B were assigned into combination of intra-vitreal bevacizumab (1.25mg/0.05ml) and triamcinolone (2mg/0.05ml) injection in the same setting. After giving

bevacizumab injection intravitreously, injection triamcinolone acetonide was given through superotemporal pars plana with same direction.

Follow-up pattern was set after 1 and 3 months of intervention. Best corrected visual acuity (BCVA) on Log MAR, central macular thickness (CMT) in microns by OCT and intraocular pressure (IOP) in mm of Hg by Goldmann Applanation Tonometer (GAT) were assessed in every visit. All the demographic, baseline and follow-up data were recorded in pre designed data collection sheet. Data were compiled, processed and presented by appropriate tables and graphs. Data were analyzed by using windows software SPSS version 23.

Results

This study was done at vitreo- retina department of NIO&H over 50 diagnosed patients of diabetic macular edema to assess the effect as well as compare the efficacy of intra-vitreal bevacizumab and macular LASER photocoagulation with combined intravitreal injection of bevacizumab and triamcinolone acetonide. Study patients were assigned with above modalities of treatment on 1:1 basis. They were followed up for two times after intervention and compared with baseline both within the groups after one month and three month and between the groups after three months follow-up.

Table-1: Comparison of mean BCVA changes at different follow up between Group- A and Group-B.

	Baseline	1st Follow-up (After 1 month)	Mean Changes After 1 month	2nd Follow-up (After 3 months)	Mean Changes After 3 months
Group-A	0.56±0.29	0.40±0.32	0.16(28.57%)	0.40±0.37	0.16(28.57%)
Group-B	0.70±0.26	0.54±0.28	0.16(22.86%)	0.45±0.36	0.25(35.71%)
P value	0.79^{ns}	0.13^{ns}		0.59^{ns}	

ns= non-significant, p value is obtained from unpaired 't'

Table-1 displayed the comparison of mean BCVA between two groups in different follow-up periods, at the beginning of the study mean visual acuity was 0.56±0.29 (SD) Log MAR unit in group A and 0.70±0.26 (SD) Log MAR unit in group B, in 1st follow-up it becomes 0.40±0.32 in group A and 0.54±0.28 (SD) in group B and mean BCVA changes are 0.16 (28.57%) for Group-A and 0.16 (22.86%) for Group-B from baseline after one month. In 2nd follow-up it becomes 0.40±0.37 (SD) in group A and 0.45±0.37 (SD) in group B and mean BCVA changes are 0.16 (22.86) and 0.25 (35.71%) respectably from baseline after three months. So, the differences of mean BCVA change between two groups after one and three months from baseline are statistically non-significant.

Table 2:Comparison of mean CMT at different follow-up visits in both groups

	Baseline	1st Follow-up (After 1 month)	Mean Changes After 1 month	2nd Follow-up (After 3 months)	Mean Changes After 3 mon.
Group-A	427.08±78.66	371.80±74.06	55.28(12.94%)	361.12±83.28	65.96(15.44%)
Group-B	482.68±122.15	411.72±114.98	70.96(14.70%)	347.52±117.00	135.16(28.0%)
P value	0.24^{ns}	0.15^{ns}		0.64^{ns}	

ns= non-significant, p value is obtained from unpaired 't' test

Table-2 showing the comparison of mean central macular thickness between two groups in different follow-up periods. At the beginning of the study mean central macular thickness was 427.08±78.67 (SD) microns in group A and 482.68±122.15 (SD) microns in group B. In 1st follow-up it becomes 371.80±74.06 (SD) microns in group A and 411.72±114.98 (SD) microns in group B and the reduction in the mean CMT from baseline is 55.28 microns (12.94%) in group A and 70.96 microns (14.70%) in group B after one month. In 2nd follow-up it becomes 361.12±83.28 (SD) microns in group A and 374.52±116.99 (SD) microns in group B and the reduction in the mean CMT from baseline is 65.96 microns (15.44%) for group A and 135.16 microns (28.0%) for group- B respectably. So, the differences of mean CMT change between two groups after one and three months from baseline are statistically non-significant.

Table 3: Distribution of comparison of mean IOP changes between two groups

	Baseline	1st Follow-up (After 1 month)	Mean Changes After 1 month	2nd Follow-up (After 3 months)	Mean Changes After 3 month
Group-A	11.80±0.71	11.60±0.58	0.20(1.96%)	11.24±0.60	0.56(4.75%)
Group-B	11.20±0.65	11.32±0.80	0.12(1.1%)	11.16±0.69	0.04(0.36%)
P value	0.003^{s}	0.16^{ns}		0.67^{ns}	

S = significant, ns = non-significant, p value obtained from unpaired 't' test

Table-3 showing the comparison of intraocular pressure changes between two groups in different follow-up periods, at the beginning of the study mean intraocular pressure was 11.80±0.71 (SD) mm (Hg) in group A and 11.20±0.65 (SD) mm of Hg in group B, in 1st follow-up it becomes 11.60±0.58 (SD) mm of Hg in group A and 11.32±0.80 (SD) mm of Hg in group B and mean IOP reduction is 0.20 mm of Hg (1.69%) for group A and mean IOP increase is + 0.12 mm of Hg (1.1%) for group B. In 2nd follow-up it becomes 11.24±0.60 (SD) mm of Hg in group A and 11.16±0.69 (SD) mm of Hg in group B and the

reduction of mean IOP are 0.56 mm of Hg (4.75%) and 0.04 mm of Hg (0.36%) respectably. At baseline, there is no significant difference of mean IOP between two groups.

Discussion

Practicing vitreo-retina specialists face many patients with visual loss associated with diabetic macular edema in their daily practice and manage them in different protocol. This prospective observational study was conducted over 50 patients of DME attending in vitreo-retina department of NIO&H who were treated by intravitreal injection of bevacizumab with laser photocoagulation (Group A) and intravitreal bevacizumab with triamcinolone acetonide injection (Group B) at 1:1 basis and the state of macular edema was assessed by OCT on baseline, after one month and after three month of intervention.

Several studies were done in different parts of the world about the management of diabetic macular edema. The different aspects of the study findings were compared and analyzed with the findings of the same aspects of the other studies.

Baseline mean BCVA was 0.57±0.29 for group- A and 0.70±0.26 for group- B which is non-significant. After one month it became 0.40±0.32 for group A and 0.54±0.28 for group B. Again, it was 0.40±0.37 for group A and 0.45±0.36 for group B after three months.

There is significant improvement of mean BCVA after one and three months within the groups from baseline. But there is no significant difference of mean BCVA improvement between two groups after one and three months of intervention. The changes of mean BCVA from baseline after one month was 0.16 (28.57%) for group-A and 0.16 (22.86%) for group-B and it was 0.16 (28.57%) for group-A and 0.25 (35.71%) for group-B after three months.

Solaiman et al. 2010 observed that there is significant improvement of BCVA after one month and three months of IVB+LASER photocoagulation. Ambade et al. 2014 observed that there is significant improvement of BCVA (0.72±0.18) after three months of combined intravitreal injection of bevacizumab and triamcinolone from baseline (0.86±0.09).

In this study there was no improvement BCVA of three patients in each group and deterioration of BCVA of three patients in group-A and two patients in group-B at final follow-up. It may be due to Poor control of DM. At final follow up there HBA1c level was investigated and it was more than normal limit (> 6.0%). It also may be due to the chronicity of the disease (DME) process. The cause should be explored.

Baseline mean CMT was 427.08±78.66 microns for group-A and 482.68±122.15 microns for group- B patients which is non-significant. In group-A patients mean CMT became 371.80±74.06 (SD) microns and 361.12±83.28 (SD) microns in 1st and 2nd follow-up periods successively. In group B patients it became 411.72±114.98 (SD) and 347.52±117.00 (SD) microns in 1st and 2nd follow-up period respectively.

There is significant reduction of mean CMT in different follow-up periods within the groups. There is more reduction of CMT in group B than group A after one month; Changes of Mean CMT is 55.28 (12.94%) for group A and 70.96 (14.70%) for group B from baseline and after three months follow up changes of mean CMT for group A was 65.96 (15.44%) and 135.16 (28.00%) for group B from baseline which is statistically non-significant.

Kamal et al. 2010 observed that there was significant reduction in the mean CMT after one- and three-months following bevacizumab and laser photocoagulation. According to the study conducted by Soheilian et al in 2009, there was significant decrease in CMT after one and three months following combined bevacizumab and triamcinolone acetonide injection. This was consistent with the current study findings.[11]

Baseline mean IOP was 11.80±0.71 mm of Hg for group- A and 11.20±0.65 mm of Hg for group-B which is statistically significant. In group A, IOP

became 11.60±0.58 mm of Hg after one month and 11.24±0.60 mm of Hg after three months follow up. In this study, the difference of baseline IOP of both groups are statistically significant that is there is no significant difference of baseline IOP between two groups. That happened as because of raised IOP was in the exclusion criteria. So, these criteria strengthened this research. But in case of group B, there was increase of IOP (11.32±0.80) from baseline (11.20±0.65) after one month due to increase IOP of two patients but it was within the normal limit (11-21 mm of Hg) and after three months. It reduced to normal without any medication.

Conclusion

Quantitative assessment and analysis of the data showed no significant difference of improvement in diabetic macular edema after treatment between intra-vitreal injections of bevacizumab with laser photocoagulation therapy and combination of intra-vitreal injection of bevacizumab with triamcinolone acetonide in most of the follow-up periods. But there was significant improvement of BCVA and CMT within the groups from baseline without affecting IOP.

Conflict of interest: None declared

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