Effects of Intravitreal Ranibizumab Injection on Diabetic Macular Edema

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ABSTRACT: Background: Diabetic macular edema (DME) is a common complication of diabetes, leading to fluid accumulation in the macula and resulting in vision impairment. With the increasing prevalence of diabetes, DME poses a significant public health challenge. Intravitreal ranibizumab, a VEGF inhibitor, has shown promise in treating DME by reducing retinal vascular permeability and improving visual outcomes. Clinical trials have demonstrated its efficacy and safety, establishing it as a key treatment option.
Aims & amp; Objectives: To evaluate the effect of intravitreal ranibizumab injection on diabetic macular oedema patients as well as on Best Corrected Visual Acuity (BCVA) and on CMT in SD-OCT.
Methodology: A prospective study was conducted among 136 patients who were suffering from Diabetic macular oedema and visited the Department of Ophthalmology, R. L. Jalappa Hospital and Research, Kolar. Data were collected in semistructured questionnarie and analysed by using SPSS software.
Results: The mean age of study participants was 56.2 years. Total 51.5% were males and remaining 48.5% were females. Mean CMT before injection was 420.5 ± 78.4 and after injection was 385.2 ± 72.1 respectively. Mean logMAR before injection was 1.045 ± 0.5 and after injection was 0.885 ± 0.48 respectively.
Conclusion: The present study concludes that a single dose of 0.5 mg of intravitreal injection of ranibizumab seems to be effective in decreasing the CMT and improving VA in patients with DME.

Keywords: *Diabetic Macular Edema, Intravitreal, Outcome, Single Dose Ranibizumab*.

INTRODUCTION:

Diabetes mellitus (DM) is a known risk factor for both microvascular and macrovascular problems [1]. Total 463 million individuals worldwide were impacted by DM in 2019; by 2030, that number is predicted to rise to 578 million [2]. Diabetic Retinopathy, which includes vitreous hemorrhage, tractional retinal detachment, diabetic macular ischaemia, and Diabetic Macular Edema, is a condition that impairs vision in diabetics [3]. Diabetic Macular Edema is the most frequent complication that has the biggest effect on a patient's quality of life out of all of them [4]. The primary molecular process responsible for DME is the phosphorylation of junctional proteins, which disrupts the blood retinal barrier [5].

Researchers hypothesized that some chemicals might be the cause of DME after they suggested that there might be a chemical that encourages vasoproliferation [6]. The discovery of VEGF, which revealed that the molecules were identical through sequencing research, confirms it. Inhibiting the single molecular target that was thought to be responsible for the formation of DME is made possible by the biochemical signal protein VEGF, which promotes angiogenesis throughout the body and eye [7, 8]. The US Food and Drug Administration (USFDA) has approved intravitreal ranibizumab as the first anti-VEGF drug. Gentech-Roche produces this recombinant humanized IgG monoclonal antibody fragment in the United States. It binds to VEGF and suppresses it. Therefore, by blocking the interaction between VEGF and its receptors, it stops the following development of new blood vessels [9].

The Food and Drug Administration (FDA) initially authorized it in 2006 for the treatment of wet age-related macular degeneration (ARMD). Since then, it has also been authorized for the treatment of macular oedema after DME and retinal vein occlusion (RVO). It was authorized for use with DR patients in 2015. The

recommended dosage for intravitreal ranibizumab varies based on indications and is either 0.3 or 0.5 mg in 0.05 mL. The actual treatment regimens, however, differ but involve rigorous monthly administration as required. Depending on the patient's condition and the doctor, injection intervals can vary, including for treating and extending a regimen. [10, 11]

Aims & Objectives:

To evaluate the effect of intravitreal ranibizumab injection on diabetic macular oedema patients as well as on Best Corrected Visual Acuity (BCVA) and on CMT in SD-OCT.

Methodology:

A prospective study was conducted among 136 patients who were suffering from Diabetic macular oedema and visited the Department of Ophthalmology, R. L. Jalappa Hospital and Research, Kolar. Patients with history of other comorbidities or Previous use of intraocular corticosteroids with in 3 months of screening as well as Patient with history of Pan-Retinal Photocoagulation (PRP) or macular laser photocoagulation or with Proliferative DR (PDR) in the study eye, iris neovascularization, vitreous haemorrhage, tractional retinal detachment, or preretinal fibrosis involving the macula in the study eye were excluded.

Using values at 95% Confidence limit and 80% power sample size of 129 was obtained in each group by using the below mentioned formula and Open epi sample size software. Expecting with 5% drop out final sample size of 129 + 7 ≈ 136 Subjects will be included in each group.

Demographic data for patients with type 2 diabetes mellitus were collected, followed by a comprehensive ocular examination, including visual acuity (Snellen and Jaeger charts), slit lamp biomicroscopy, and fundus examination. Spectral- domain optical coherence tomography (SD-OCT) images were obtained prior to the intravitreal injection of ranibizumab (0.5 mg), administered under sterile conditions. Follow-up assessments were occurred on day 0, day 1, and at 1 week, 1 month, 2 months, and 3 months, focusing on visual acuity and cystoid macular thickness (CMT) via SD-OCT. The Institutional Ethical committee permission was taken prior to the study.

Data entry & analysis:

Data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS version 25.0 (SPSS Inc., Chicago, IL, US). Paired t-tests assessed differences in means for independent samples, comparing the mean values of cystoid macular thickness (CMT) and visual acuity (VA) before and after the intervention, with a p-value of <0.05 considered statistically significant. Additionally, Pearson's correlation coefficient evaluated the correlation between CMT and VA.

RESULTS:

Total 136 patients were included in the study. The mean age of study participants was 56.2 years. Total 51.5% were males and remaining 48.5% were females. Mean CMT before injection was 420.5 ± 78.4and after injection was 385.2 ± 72.1 respectively. There was stastically significant difference found between mean CMT before and after injection. Mean logMAR before injection was 1.045 ± 0.5and after injection was 0.885 ± 0.48, respectively. There was stastically significant difference found between mean CMT before and after injection.[Table -1].

Table 1: Distribution of mean CMT and LogMAR (Visual Acuity) for 136 samples (70 males and 66 females) before and after injection of ranibizumab.

Parameters	Mean±SD	Minimum	Maximum	Median	p-value
CMT before injection (µm)	420.5 ± 78.4	290.00	640.00	417.00	<0.0001
CMT after injection (µm)	385.2 ± 72.1	270.00	570.00	362.00	<0.0001
LogMAR before injection (logunits)	1.045 ± 0.5	0.20	2.50	1.00	<0.0001
LogMAR after injection (logunits)	0.885 ± 0.48	0.20	2.40	0.78	<0.0001

Table 2: Correlation of CMT and logMAR (Visual Acuity) before and after injection ranibizumab.

Metric	CMT Before Injection	CMT After injection	logMAR Before Injection	logMAR After Injection
Pearson's Correlation Coefficient (r)	0.069	0.56	0.078	0.054
p-value	0.634	0.687	0.5640	0.645
Sample Size(n)	136	136	136	136

A positive correlation was found between CMT as well as LogMAR before and after injection.[Table 2].

Table 3: Correlation between logMAR before injection

Parameters	CMT before injection ranibizumab	
logMAR before injection	Pearson's correlation coefficient(r)	0.854
	p-value	<0.0001
	Number(N)	136

Table 4: Correlation between logMAR after injection ranibizumab vs CMT after injection ranibizumab.

Parameters	CMT after Injection ranibizumab	
logMAR after injection	Pearson's correlation coefficient(r)	0.868
	p-value	<0.0001
	Number(N)	136

The value of Pearson's correlation coefficient (r) was 0.0854. A high positive correlation was found between logMAR before injection ranibizumab vs CMT before injection ranibizumab.[Table 3]. The value of Pearson's correlation coefficient (r) was 0.868. High positive correlation was found between logMAR after injection ranibizumab vs CMT after injection ranibizumab [Table 4].

DISCUSSION:

The current study included 136 patients in total. The mean logMAR VA improved from 0.52±0.34 at baseline to 0.44±0.32 at one month following treatment, according to Inagaki K et al. By one month, the mean CMT dropped considerably [12].

According to Minami Y et al., after two hours, the mean FT dropped dramatically from 452±77 to 429±65 µm. The mean logarithm of the minimal angle of resolution BCVA showed a notable improvement. There was a substantial correlation between the ΔFT after two hours and the ΔFT after a month. There was a substantial correlation between the ΔVA after one day and the ΔVA after one month [13]. According to Campochiaro PA et al., there are a number of cytokines with varying amounts in the aqueous humor between DME and macular oedema following Branch Retinal Vein Occlusion (BRVO) [14]. According to the authors, assessing the short-term intravitreal injection effects of ranibizumab will help predict the drug's efficacy and take into account the differences in the mechanisms of macular oedema between BRVO and DME by measuring the intraocular cytokine levels in the eyes.

According to Sharaf A et al. study, the mean CMT before injection was 432.0±144.0 µm, and at one month, it was 341.0±88.66 µm, with a 17.96% improvement [15]. In the current study, CMT preinjection was 416.0095±93.3345 µm and one month postinjection was 383.8667±90.2228 µm, with Pearson's correlation coefficient being 0.061 and 0.052 suggesting a positive correlation.

In a previous investigation, Welch DE et al. found that the FT dramatically decreased in two patients with exudative Age-related Macular Degeneration (AMD) and seven patients with DME one to two hours after intravitreal injection of bevacizumab (IVB) [16]. They noted a notable reduction in OCT thickness within two hours after injection. The current findings are consistent with their study, even though patients with DME and AMD were treated with bevacizumab, a different anti-VEGF medication. Baseline FT was said to be able to predict the structural outcome in response to IVR therapy [17]. Additionally, there was a strong association between the baseline BCVA and the BCVA one month later. According to earlier reports, baseline BCVA may be able to predict the functional outcome following IVR treatment [18, 19].

CONCLUSION:

The present study concludes that a single dose of 0.5 mg of intravitreal injection of ranibizumab seems to be effective in decreasing the CMT and improving VA in patients with DME. The need for the present study was to evaluate the effect of single dose injection ranibizumab in patients with DME which was achieved.

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