

Research Article

Comparative Study to Evaluate Efficacy and Safety of Intravitreal Injections of Bevacizumab and Ranibizumab in Patients of Diabetic Macular Edema in a Tertiary Care Hospital

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ABSTRACT

Introduction: Diabetes mellitus is a chronic metabolic disorder driven by hyperglycemia and insulin resistance which can lead to microvascular complications like diabetic macular edema (DME) - a primary cause of blindness in the working-age population. The pathophysiology of DME involves blood-retinal barrier breakdown and elevated vascular endothelial growth factor levels. While anti-VEGF therapies have transformed management, comparing agents like Bevacizumab and Ranibizumab remains clinically relevant.

Objectives: To evaluate and compare the safety and efficacy of intravitreal Bevacizumab versus Ranibizumab in patients with DME over a 16-week period. To measure the proportion of patients achieving ≥ 15 ETDRS letter improvements and assessing mean changes in central subfield thickness.

Material and Methods: A prospective, open-labelled, comparative study was conducted over 16 weeks on 130 newly diagnosed DME patients divided equally into Group A (n=65) received monthly intravitreal Bevacizumab (1.25 mg/0.05 mL) and Group B (n=65) received monthly intravitreal Ranibizumab (0.5 mg/0.05 mL). Baseline evaluations included BCVA via ETDRS charts, OCT imaging for CST and comprehensive systemic laboratory profiles. Data were analysed using SPSS 22.0 with Student's t-tests and Chi-square tests ($p < 0.05$).

Results: At 16 weeks both groups showed significant improvements in BCVA ($p < 0.001$), though Ranibizumab demonstrated better visual gains (67.5 ± 11.0 vs. 61.2 ± 10.4 letters; $p = 0.003$) and a higher proportion of patients achieving ≥ 15 letter gains (47.7% vs. 27.7%; $p = 0.019$). Mean CST decreased significantly in both groups ($p < 0.001$), with Ranibizumab showing a greater reduction ($-152.8 \pm 48.6 \mu\text{m}$ vs. $-117.8 \pm 45.3 \mu\text{m}$; $p < 0.01$). Ocular adverse events were mild and transient. No severe complications or systemic/thromboembolic events reported and metabolic parameters remained stable ($p > 0.05$).

Conclusion: Both intravitreal Bevacizumab and Ranibizumab are safe and effective for managing DME, with Ranibizumab demonstrating better short-term visual and anatomical efficacy while Bevacizumab remains a reliable, economical alternative.

Keywords: Diabetic Macular Edema, Bevacizumab, Ranibizumab.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance, impaired insulin secretion or both. In 2015 the International Diabetes Federation reported that 415 million individuals aged 20 to 79 were diagnosed with diabetes mellitus¹.

An extra 200 million individuals are projected to develop diabetes by 2040, making the illness a significant global public health issue. Chronic hyperglycemia and other metabolic problems in diabetes mellitus patients might impair many organ systems. This may result in severe and sometimes fatal health problems including microvascular (retinopathy,

nephropathy and neuropathy) and macrovascular (two to four fold greater risk of cardiovascular illnesses).

Organ failure resulting from or exacerbated by chronically elevated blood glucose levels is a defining characteristic of diabetes mellitus (DM). Macrovascular and microvascular problems describe the long-term health consequences of diabetes. Diabetes is the only condition recognized for inducing the microvascular triad of ocular impairment, renal damage and neuropathy². Most patients with diabetes develop manifestations of microvascular disease over time.

Prolonged exposure of tissue to hyperglycemia is the primary cause of microvascular disease. The 1998 trial³ on Intensive Blood-Glucose Control with Sulphonylureas and the 1993 study⁴ on the Impact of Intensive Diabetes Treatment on Long-Term Complications in Insulin-Dependent Diabetes Mellitus are important clinical investigations that have established a definitive correlation between microvascular disease and glucose regulation. Additional significant studies are the Diabetes Control and Complications Trial (DCCT)⁵ and the UK Prospective Diabetes Study (UKPDS)⁶. The kidney, retina and vascular endothelium are tissues in which glucose uptake is independent of insulin action. This is due to these tissues exhibiting glucose levels that are strongly associated with blood glucose levels, making them more likely to develop microvascular disease. Hyperglycemia induces oxidative stress due to excessive superoxide generation, direct endothelial damage mediated by glucose and the synthesis of sorbitol and advanced glycation end-products⁷. Injuries to the metabolic system result in changes to blood flow, endothelial permeability, extravascular protein accumulation and coagulation, all of which contribute to organ failure. A study clearly indicates a link between hypertension and the progression of nephropathy and retinopathy⁸. There is now definitive evidence that they independently contribute to the progression of microvascular disease.

Most occurrences of blindness due to diabetes are linked to diabetic macular edema (DME). Although spontaneous recovery is rather rare, DME often manifests as a chronic illness. Approximately after six months without therapy diabetic macular edema resolves spontaneously in around one-third of the patients. Numerous systemic factors including hypertension, dyslipidemia, nephropathy and

inadequately managed diabetes metabolism are now believed to have a role in the disease's progression⁹.

Objectives:

The aim of this study is to compare the safety and efficacy of intravitreal injections of bevacizumab versus ranibizumab in patients with diabetic macular edema over 16 weeks. To evaluate and compare the individual and relative efficacy and safety profiles of both drugs. To determine the proportion of patients achieving a significant visual improvement of greater than 15 ETDRS letters and to measure the mean change in Optical Coherence Tomography central subfield thickness at 16 weeks.

MATERIAL AND METHODS:

A prospective, open-labelled, comparative study conducted in 2025 at a tertiary care center (Department of Pharmacology in collaboration with the Department of Ophthalmology) on 130 patients newly diagnosed with DME and divided equally into two parallel treatment arms (n = 65 per group). Group A: Received intravitreal bevacizumab (1.25 mg/0.05 mL) monthly in the trial eye for 16 weeks. Group B: Received intravitreal ranibizumab (0.5 mg/0.05 mL) monthly in the trial eye for 16 weeks. Patients aged >18 years with clinically diagnosed DME, baseline Best Corrected Visual Acuity (BCVA) ETDRS score between 78 and 19 letters and an OCT central subfield thickness (CST) of >320µm were included. Patient with non-diabetic macular edema, prior intraocular treatment within 90 days, active ocular inflammation or infection, uncontrolled glaucoma, uncontrolled hypertension, or recent acute coronary events were excluded.

The study was conducted after obtaining approval from Institutional Ethical Committee (IEC Ref: 02555/ACAD-III/MCA/2024). Patients underwent comprehensive baseline evaluations, including demographic details, BCVA testing using ETDRS charts, OCT imaging for CST and retinal morphology, and systemic lab investigations (CBC, HbA1c, RFT, LFT, serum electrolytes and lipid profiles). Follow-ups were conducted monthly for 16 weeks to monitor visual and anatomical outcomes alongside ocular and systemic safety parameters.

Data were analysed using SPSS version 22.0. Continuous variables were expressed as mean±standard deviation and compared using Student's t-tests, while categorical variables

were assessed using the Chi-square test ($p < 0.05$ considered statistically significant).

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics of Patients with Diabetic Macular Edema

Baseline Parameter	Group A (Bevacizumab, n=65)	Group B (Ranibizumab, n=65)	Total / p-value
Mean Age (Years)	54.8±8.6	55.2±8.9	—
Gender Distribution (Male)	41(63.1%)	39(60.0%)	61.5% overall
Baseline BCVA (ETDRS Letters)	52.4±9.8	53.1±10.1	$p = 0.68$
Baseline CST (μm)	468.2±82.5	472.9±85.1	$p = 0.74$

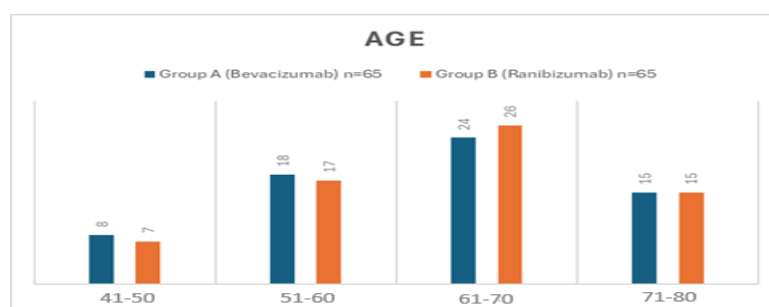


Fig 4.1 Age distribution of the patients

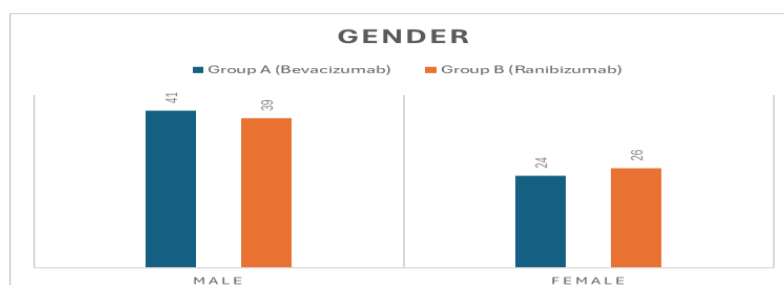


Fig 4.2 Gender distribution of patients

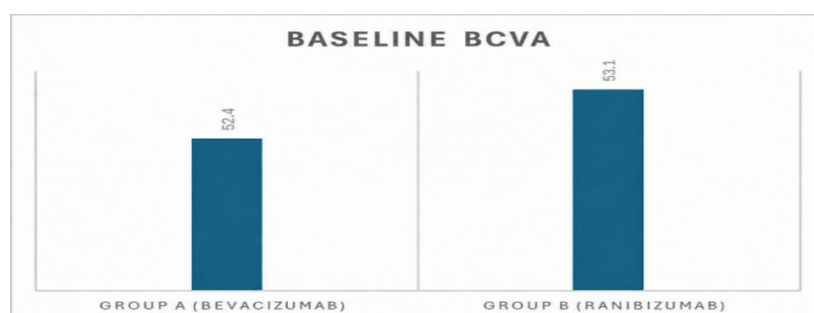


Fig 4.3: Baseline Best Corrected Visual Acuity (ETDRS Letters)

Table 2: Comparison of Visual Acuity Outcomes (BCVA in ETDRS Letters) Between Treatment Groups at 16 Weeks

Efficacy Parameter	Group A (Bevacizumab, n=65)	Group B (Ranibizumab, n=65)	p-value
Baseline BCVA (ETDRS Letters)	52.4±9.8	53.1±10.1	0.68
16-Week BCVA (ETDRS Letters)	61.2±10.4	67.5±11.0	0.003 (Between groups)

Intragroup BCVA Improvement	p < 0.001	p < 0.001	—
Patients with ≥ 15 Letters Gain	18 (27.7%)	31 (47.7%)	0.019

Fig 4.4: Visual Acuity Improvement at 16 Weeks (ETDRS Letters)

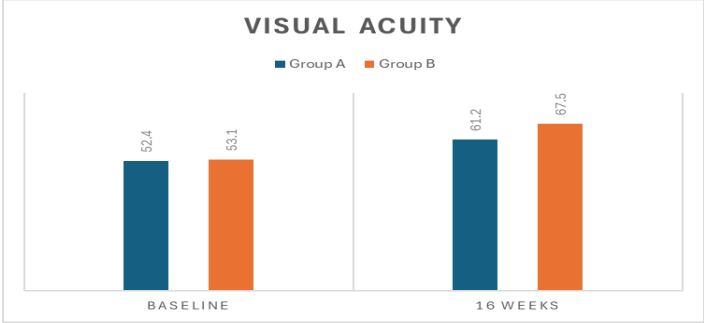


Fig 4.5: Proportion of the patients with ≥ 15 ETDRS Letters Improvement

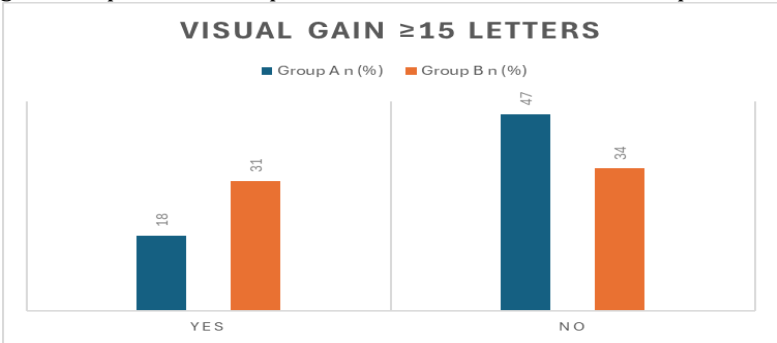


Table 3: Comparison of Central Subfield Thickness (CST) and Anatomical Outcomes between Treatment Groups at 16 Weeks

Anatomical Parameter	Group A (Bevacizumab, n=65)	Group B (Ranibizumab, n=65)	p-value
Baseline CST (μm)	468.2 $\pm$ 82.5	472.9 $\pm$ 85.1	0.74
16-Week CST (μm)	350.4 $\pm$ 78.6	320.1 $\pm$ 74.9	0.01 (Between groups)
Mean Reduction in CST (μm)	-117.8 $\pm$ 45.3	-152.8 $\pm$ 48.6	< 0.01
Intragroup CST Reduction	p < 0.001	p < 0.001	—

Fig 4.7: Change in OCT Central Subfield Thickness at 16 Weeks

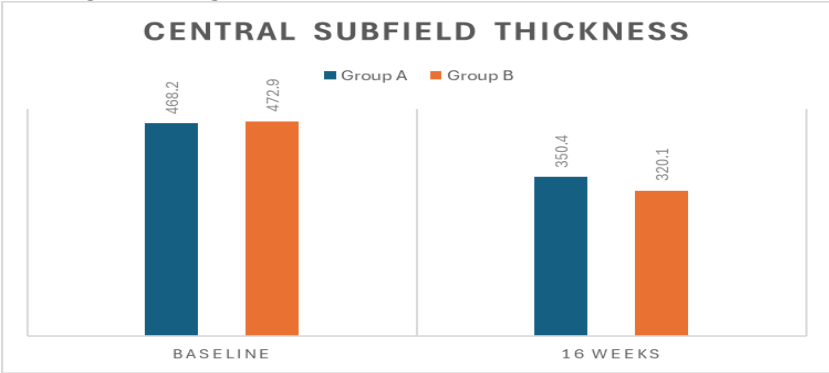


Table 4: Comparison of Ocular Adverse Events, Systemic Complications and Laboratory Parameters between Treatment Groups

Safety and Laboratory Parameter	Group A (Bevacizumab,	Group B (Ranibizumab,	p-value
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	n=65)	n=65)	
Intraocular Inflammation	2 (3%)	1 (1.5%)	> 0.05 (1.000)
Raised IOP	3 (4.6%)	1 (1.5%)	> 0.05 (0.619)
Subconjunctival Haemorrhage	2 (3%)	2 (3%)	> 0.05 (1.000)
Eye Pain and Irritation	1 (1.5%)	1 (1.5%)	> 0.05 (1.000)
Severe Complications (Endophthalmitis / Detachment)	0 (0%)	0 (0%)	—
Systemic / Thromboembolic Events	0 (0%)	0 (0%)	—
Hematological, Glycemic (HbA1c), & Renal Parameters	Remained stable	Remained stable	> 0.05 (Not significant)

DISCUSSION

Baseline Demographics and Clinical Characteristics (Table 1)

In the present study evaluating 130 patients with diabetic macular edema (DME), baseline demographic and clinical features were well-balanced between the two treatment arms. The mean age of patients was 54.8 ± 8.6 years in Group A (Bevacizumab) and 55.2 ± 8.9 years in Group B (Ranibizumab) with an overall male predominance of 61.5%. These demographic metrics align closely with findings reported by Ozturk et al. (2011)¹⁰, who observed a mean patient age of 56.18 ± 13.07 years when comparing intravitreal bevacizumab and ranibizumab in DME. The landmark DRCR.net Protocol T study by Wells et al. (2015)¹¹ reported a mean patient age of 61 ± 10 years among patients receiving intravitreal aflibercept, bevacizumab and ranibizumab for DME showing that DME predominantly affects the middle-aged and elderly population. Baseline disease severity indicators showed no statistically significant differences between our cohorts, with initial best-corrected visual acuity (BCVA) recorded at 52.4 ± 9.8 ETDRS letters in Group A and 53.1 ± 10.1 letters in Group B ($p = 0.68$). Similarly, baseline central subfield thickness (CST) was comparable ($468.2 \pm 82.5 \mu\text{m}$ vs. $472.9 \pm 85.1 \mu\text{m}$; $p = 0.74$), matching baseline thickness ranges observed in the study of Brown et al. (2013)¹² RISE and RIDE phase III clinical trials ($450\text{--}470 \mu\text{m}$). This balanced baseline comparability ensures that subsequent therapeutic differences are most likely from the pharmacologic agents rather than confounding pre-existing variations.

Visual Acuity and Functional Outcomes (Table 2)

Over the 16-week period, both treatment regimens produced significant improvements

in functional visual acuity ($p < 0.001$). The patients treated with Ranibizumab achieved a significantly superior visual gain (67.5 ± 11.0 letters) compared to those receiving Bevacizumab (61.2 ± 10.4 letters) showing a statistically significant between-group difference ($p = 0.003$). A significantly greater proportion of patients in Group B achieved a clinically meaningful gain of ≥ 15 ETDRS letters (47.7%, $n=31$) compared to Group A (27.7%, $n=18$; $p = 0.019$). These findings are supported by the DRCR.net Protocol T trial which demonstrated higher functional visual improvements with Ranibizumab in short-term DME management. While large-scale trials like the CATT trial (CATT Research Group. 2011)¹³ and IVAN trial (Chakravarthy et al., 2013)¹⁴ studies reported comparable long-term visual outcomes between bevacizumab and ranibizumab under specific flexible dosing schedules, our findings support the evidence that ranibizumab frequently provides a more significant and rapid short-term functional recovery.

Anatomical Outcomes and CST Reduction (Table 3)

Anatomical evaluation via Optical Coherence Tomography (OCT) demonstrated significant reductions in macular edema for both cohorts at 16 weeks ($p < 0.001$). Group A experienced a mean CST reduction of $-117.8 \pm 45.3 \mu\text{m}$ (decreasing from a baseline of $468.2 \pm 82.5 \mu\text{m}$ to $350.4 \pm 78.6 \mu\text{m}$). In comparison, Group B achieved a significantly greater mean CST reduction of $-152.8 \pm 48.6 \mu\text{m}$ (decreasing from $472.9 \pm 85.1 \mu\text{m}$ to $320.1 \pm 74.9 \mu\text{m}$), with the intergroup difference reaching statistical significance ($p = 0.01$). These results correlate with Ozturk et al. (2011)¹⁰ who found that to a larger degree, macular thickness was reduced with Ranibizumab than with Bevacizumab in

diabetic macular edema patients. Heier et al. (2012)¹⁵ showed significant anatomical improvements with Ranibizumab therapy and Elman et al. (2010)¹⁶ presented a long-term decrease in retinal thickness with anti-VEGF therapy. All these studies contribute to the increased potential of Ranibizumab in reducing macular edema.

Safety Profile and Laboratory Parameters (Table 4)

Both intravitreal agents exhibited favourable and statistically comparable ocular and systemic safety profiles ($p > 0.05$). Ocular adverse events were predominantly mild, transient and managed conservatively. Intraocular inflammation occurred in 2 patients (3%) in Group A and 1 patient (1.5%) in Group B ($p > 0.05$), while transiently raised intraocular pressure was observed in 3 patients (4.6%) and 1 patient (1.5%), respectively ($p > 0.05$). Subconjunctival haemorrhage (3%) and mild eye irritation (1.5%) incidence rates were identical or comparable across groups. There were no severe sight-threatening complications—such as endophthalmitis, retinal detachment, or retinal tears—were recorded in either cohort, confirming that strict aseptic techniques effectively minimize procedural risks. Systemically, no cardiovascular or thromboembolic adverse events were reported. Comprehensive laboratory investigations, including hematological parameters, glycemic control markers (HbA1c and random blood sugar) and renal function profiles (serum creatinine and blood urea), remained stable throughout the 16 weeks without clinically relevant variations ($p > 0.05$). These findings are consistent with the CATT trial (CATT Research Group. 2011)¹³. Clinically significant systemic adverse events were not observed during the 16-week period; however, the sample size and duration of follow-up may not be sufficient to detect rare or delayed systemic adverse events.

CONCLUSION

Intravitreal administration of Bevacizumab and Ranibizumab are both safe and effective therapeutic strategies for managing diabetic macular edema. In this study, ranibizumab demonstrated greater short-term improvement in BCVA and CST compared with bevacizumab in improving visual acuity and reducing macular thickness. Bevacizumab serves as a safe alternative. Treatment selection should

integrate clinical severity, retinal architecture and patient-specific economic factors to optimize real-world visual outcomes.

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