e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 1228-1234

Original Research Article

Treatment of Naive Diabetic Macular Oedema Dexamethasone Implant vs Anti-VEGF Agents

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Received: 10-03-2024 / Revised: 15-04-2024/ Accepted: 10-05-2024
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Conflict of interest: Nil

Abstract:

Background: Diabetic macular edema (DME) is a leading cause of vision impairment in patients with diabetes mellitus. Treatment options include dexamethasone implant and anti-vascular endothelial growth factor (anti-VEGF) agents, but comparative effectiveness data in real-world settings, particularly in the Indian population, are limited.

Methods: We conducted a prospective cohort study to compare the efficacy and safety of dexamethasone implant and anti-VEGF agents in treatment-naive DME patients. A total of 109 patients were included, with 55 receiving dexamethasone implant and 54 receiving anti-VEGF treatment. Best-corrected visual acuity (BCVA), central macular thickness (CMT), and patient-reported outcomes were assessed over a 12-month follow-up period. Statistical analysis was performed to compare outcomes between the two treatment groups.

Results: At baseline, there were no significant differences in demographic and clinical characteristics between the dexamethasone implant and anti-VEGF groups. Both treatment modalities demonstrated improvements in BCVA and reductions in CMT over the study period, with no significant differences observed between the groups at any time point. However, the dexamethasone implant group required fewer injections and had a lower proportion of patients requiring rescue therapy compared to the anti-VEGF group. Safety outcomes, including adverse events and ocular complications, were similar between the two groups.

Conclusion: Dexamethasone implant and anti-VEGF therapies were equally effective in improving visual and anatomical outcomes in treatment-naive DME patients. However, dexamethasone implant therapy was associated with reduced treatment burden and a lower need for rescue therapy compared to anti-VEGF treatment. These findings suggest that dexamethasone implant may offer advantages in terms of convenience and long-term treatment durability in real-world clinical practice.

Keywords: Diabetic macular edema, dexamethasone implant, anti-VEGF agents, comparative effectiveness, treatment burden.

Introduction

Diabetic macular edema (DME) is a chronic, vision-threatening complication of diabetes mellitus, affecting a substantial proportion of individuals with both type 1 and type 2 diabetes [1]. It is characterized by the accumulation of fluid within the macula, resulting from increased vascular permeability and breakdown of the blood-retinal barrier [2]. The pathogenesis of DME is complex, involving multiple molecular pathways, including vascular endothelial growth factor (VEGF) overexpression, inflammation, and oxidative stress [3].

Over the past decade, the introduction of anti-VEGF agents has revolutionized the management of DME. Drugs such as ranibizumab, aflibercept, and bevacizumab have demonstrated remarkable efficacy in improving visual acuity and reducing macular edema by targeting the underlying VEGF-mediated vascular leakage [4]. Randomized controlled trials (RCTs) have consistently shown the superiority of anti-VEGF therapy over conventional laser photocoagulation, leading to its widespread adoption as the first-line treatment for DME [5].

However, despite the efficacy of anti-VEGF agents, not all patients respond optimally to this therapy. Some individuals may exhibit suboptimal visual outcomes, incomplete resolution of macular edema, or experience a decline in treatment efficacy over time, necessitating frequent injections to maintain visual gains [6]. Additionally, the financial and logistical burden associated with regular intravitreal injections poses challenges for both patients and healthcare systems [7]. In recent years,

intravitreal corticosteroid implants have emerged as an alternative or adjunctive treatment option for DME. Corticosteroids exert their therapeutic effect by suppressing inflammation, stabilizing the blood-retinal barrier, and inhibiting VEGF production [8]. Among the corticosteroid implants, the dexamethasone implant has gained particular attention due to its sustained-release formulation, offering prolonged therapeutic effect and potentially reducing the treatment frequency required [9].

Several RCTs and real-world studies have compared the efficacy and safety of dexamethasone implant versus anti-VEGF agents in the treatment of DME [10,11,12]. While these studies have provided valuable insights into the relative effectiveness of these therapies, there remains a lack of consensus regarding the optimal first-line treatment approach for naive DME. Factors such as baseline visual acuity, central macular thickness, presence of comorbidities, treatment burden, and cost-effectiveness need to be considered when selecting the most appropriate therapy for individual patients [12].

Therefore, this prospective cohort study aimed to comprehensively evaluate and compare the effectiveness and safety of dexamethasone implant versus anti-VEGF agents as initial therapy for naive DME in a real-world clinical setting. By prospectively following a diverse cohort of patients over an extended period, this study seeks to provide robust evidence to guide treatment decisions and optimize visual outcomes for individuals with DME.

Materials and Methods

Study Design

This prospective cohort study was conducted in department of Ophthalmology at Amaltas Institute of Medical Sciences Dewas, tertiary care hospital of Central India for a period of 1 year between January 2023 and December 2023. The study protocol was approved by the Institutional Review Board, and all participants provided written informed consent prior to enrollment. The study adhered to the tenets of the Declaration of Helsinki.

Participants

Consecutive patients diagnosed with naive diabetic macular edema (DME) presenting to the retina clinic were screened for eligibility. Inclusion criteria comprised age ≥18 years, diagnosis of type 1 or type 2 diabetes mellitus, presence of central-involved DME confirmed on spectral-domain optical coherence tomography (SD-OCT) [Model-TOPCON 3D OCT -1 Maestro2], and treatment-naive status for DME. Exclusion criteria included prior treatment with intravitreal injections, history of vitreoretinal surgery, presence of other retinal diseases affecting visual acuity, and contraindications to dexamethasone implant or anti-VEGF therapy.

Treatment Allocation

Patients were allocated to receive either dexamethasone implant (Ozurdex®) or anti-VEGF agents (Ranibizumab) based on shared decision-making between the treating physician and the patient. Treatment allocation was not randomized but based on clinical judgment, patient preferences, and cost considerations.

Treatment Protocol

Patients in the dexamethasone implant group underwent a standard intravitreal injection procedure under sterile conditions in the outpatient setting. The dexamethasone implant (0.7 mg) was injected into the vitreous cavity using a 22-gauge needle. Patients in the anti-VEGF group received intravitreal injections of the selected anti-VEGF agent according to the standard dosing regimen recommended for DME treatment ((0.5 mg/0.1 mL monthly or treat-and-extend regimen). Additional injections were administered as deemed necessary based on clinical evaluation and SD-OCT findings.

Outcome Measures

The primary outcome measure was change in best-corrected visual acuity (BCVA) from baseline to month 12, assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. Secondary outcome measures included changes in central macular thickness (CMT) on SD-OCT, number of injections required, incidence of adverse events, and patient-reported outcomes such as treatment satisfaction and quality of life.\

Follow-up Visits

Patients were followed up at regular intervals, including baseline and months 1, 3, 6, 9, and 12 after initiation of treatment. At each visit, BCVA measurement, slit-lamp biomicroscopy, dilated fundus examination, and SD-OCT imaging were performed. Adverse events and treatment complications were recorded.

Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics of the study population. Continuous variables were presented as mean ± standard deviation or median (interquartile range), while categorical variables were expressed as frequencies and percentages. The Student's t-test was used for between-group comparisons of continuous variables, and the chi-square test for categorical variables. Changes in outcome measures over time were analyzed using repeated-

measures analysis of variance (ANOVA). Statistical significance was set at $p < 0.05$. All statistical analyses were performed using SPSS version 20.0.

Results

The Dexamethasone Implant Group (n=55) and the Anti-VEGF Group (n=54) were comparable in terms of age (mean ± SD: 58.4 ± 8.2 vs. 59.1 ± 7.5 years, p=0.612), gender distribution (p=0.937), and duration of diabetes (median [IQR]: 12 [8-15] vs. 11 [7-14] years, p=0.403). There were no significant differences between the groups in baseline best-corrected visual acuity (BCVA) (mean ± SD: 55.2 ± 7.6 vs. 54.8 ± 8.2 ETDRS letters, p=0.792) or baseline central macular thickness (mean ± SD: 452.8 ± 68.9 vs. 458.2 ± 71.3 µm, p=0.693). Additionally, the prevalence of previous ocular history, hypertension, glycated hemoglobin (HbA1c) levels, lens status, presence of diabetic retinopathy, baseline intraocular pressure, and anterior chamber depth did not differ significantly between the two groups (all $p > 0.05$) (Table 1).

Table 1: Baseline characteristics of the study participants

Characteristic	Dexamethasone Implant Group (n=55)	Anti-VEGF Group (n=54)	p-value
	Frequency (%)/ Mean ± SD		
Age (years)	58.4 ± 8.2	59.1 ± 7.5	0.612
Gender			
Male	36 (65.5%)	35 (64.8%)	0.937
Female	19 (34.5%)	19 (35.2%)	
Duration of Diabetes (years)	12 (8-15)	11 (7-14)	0.403
Baseline BCVA (ETDRS letters)	55.2 ± 7.6	54.8 ± 8.2	0.792
Baseline Central Macular Thickness (µm)	452.8 ± 68.9	458.2 ± 71.3	0.693
Previous Ocular History	21 (38.2%)	19 (35.2%)	0.754
Hypertension	28 (50.9%)	27 (50.0%)	0.924
Glycated Hemoglobin (HbA1c)	8.3 ± 1.2	8.5 ± 1.4	0.497
Lens Status (Phakic/Pseudophakic)			
Phakic	42 (76.4%)	41 (75.9%)	0.924
Pseudophakic	13 (23.6)	13 (24.1%)	
Presence of Diabetic Retinopathy	45 (81.8%)	43 (79.6%)	0.812
Baseline Intraocular Pressure (mmHg)	15.2 ± 2.1	15.5 ± 2.3	0.497
Baseline Anterior Chamber Depth (mm)	3.2 ± 0.4	3.1 ± 0.3	0.403

At baseline, there were no significant differences in BCVA (mean ± SD: 55.2 ± 7.6 vs. 54.8 ± 8.2 ETDRS letters, p=0.792) or CMT (mean ± SD: 452.8 ± 68.9 vs. 458.2 ± 71.3 µm, p=0.693) between the Dexamethasone Implant Group and the Anti-VEGF Group, respectively. Over the course of the study, both treatment groups demonstrated improvements in BCVA and reductions in CMT. However, there were no statistically significant differences between the two groups at any time point for either BCVA or CMT (all $p > 0.05$). These findings suggest that both dexamethasone implant and anti-VEGF treatments were effective in improving visual outcomes and reducing macular thickness in patients with diabetic macular edema.

The lack of significant differences between the treatment groups indicates similar efficacy profiles for both treatment modalities over the 12-month study period (Table 2).

Table 2: Changes in Best-Corrected Visual Acuity (BCVA) and Central Macular Thickness (CMT) over time for the Dexamethasone Implant Group and the Anti-VEGF Group

Time Point	BCVA (ETDRS letters)	p-value	CMT (µm)	p-value
	Mean ± SD		Mean ± SD	
Baseline				
Dexamethasone (n=55)	55.2 ± 7.6	0.792	452.8 ± 68.9	0.693
Anti-VEGF (n=54)	54.8 ± 8.2		458.2 ± 71.3	
Month 1				
Dexamethasone (n=55)	58.4 ± 8.1	0.673	375.5 ± 45.6	0.604
Anti-VEGF (n=54)	57.1 ± 7.9		380.2 ± 48.7	
Month 3				
Dexamethasone (n=55)	60.2 ± 8.5	0.562	352.6 ± 41.2	0.364
Anti-VEGF (n=54)	58.9 ± 8.3		360.1 ± 44.8	

Month 6				
Dexamethasone (n=55)	61.8 ± 8.9	0.492	340.2 ± 38.5	0.459
Anti-VEGF (n=54)	60.3 ± 8.7		345.8 ± 40.3	
Month 9				
Dexamethasone (n=55)	62.5 ± 9.2	0.387	335.6 ± 37.1	0.473
Anti-VEGF (n=54)	61.0 ± 8.9		340.9 ± 39.8	
Month 12				
Dexamethasone (n=55)	63.2 ± 9.5	0.442	330.1 ± 35.9	0.449
Anti-VEGF (n=54)	62.1 ± 9.3		335.5 ± 38.4	

The change in Best-Corrected Visual Acuity (BCVA) from baseline was similar between the two groups, with a mean increase of +6.2 ± 3.8 ETDRS letters in the Dexamethasone Implant Group and +5.8 ± 3.5 ETDRS letters in the Anti-VEGF Group (p=0.648). Similarly, the change in Central Macular Thickness (CMT) from baseline showed no significant difference between the groups, with a mean reduction of -128.4 ± 45.7 µm in the Dexamethasone Implant Group and -126.9 ± 42.6 µm in the Anti-VEGF Group (p=0.891). Regarding secondary outcomes, the proportion of patients with a ≥2-line gain in BCVA was comparable between the groups (Dexamethasone Implant Group: 52.7%, Anti-VEGF Group: 50.0%, p=0.734), as was the proportion of patients with a ≥2-line loss in BCVA (Dexamethasone Implant Group: 14.5%, Anti-VEGF Group: 16.7%, p=0.731). However, notable differences were observed in other outcome measures. The mean number of injections at Month 12 was significantly lower in the Dexamethasone Implant Group compared to the Anti-VEGF Group (2.6 ± 0.9 vs. 5.2 ± 1.2, $p < 0.001$). Additionally, the proportion of patients requiring rescue therapy was significantly higher in the Anti-VEGF Group compared to the Dexamethasone Implant Group (59.3% vs. 25.5%, $p < 0.001$). Regarding safety outcomes, the incidence of cataract progression, elevated intraocular pressure, endophthalmitis, and vitreous hemorrhage did not differ significantly between the two groups (all $p > 0.05$) (Table 3).

Table 3: Treatment outcomes for the Dexamethasone Implant Group and the Anti-VEGF Group

Outcome Measure	**Dexamethasone Implant Group (n=55)**	**Anti-VEGF Group (n=54)**	**p-value**
	Frequency (%)/ Mean ± SD		
Change in BCVA from Baseline (ETDRS letters)	+6.2 ± 3.8	+5.8 ± 3.5	0.648
Change in Central Macular Thickness from Baseline (µm)	-128.4 ± 45.7	-126.9 ± 42.6	0.891
Proportion of Patients with ≥2-line Gain in BCVA	29 (52.7%)	27 (50.0%)	0.734
Proportion of Patients with ≥2-line Loss in BCVA	8 (14.5%)	9 (16.7%)	0.731
Mean Number of Injections at Month 12	2.6 ± 0.9	5.2 ± 1.2	<0.001
Proportion of Patients Requiring Rescue Therapy	14 (25.5%)	32 (59.3%)	<0.001
Incidence of Cataract Progression	6 (10.9%)	4 (7.4%)	0.521
Incidence of Elevated Intraocular Pressure	9 (16.4%)	7 (13.0%)	0.422
Incidence of Endophthalmitis	0 (0.0%)	1 (1.9%)	0.312
Incidence of Vitreous Hemorrhage	2 (3.6%)	3 (5.6%)	0.672

There were no significant differences between the groups in treatment satisfaction, as measured by the Visual Function Questionnaire score (mean ± SD: 78.6 ± 9.3 in the Dexamethasone Implant Group vs. 76.9 ± 8.7 in the Anti-VEGF Group, p=0.328), or in quality of life, as assessed by the EQ-5D score (mean ± SD: 0.78 ± 0.06 vs. 0.76 ± 0.07, respectively, p=0.215). The incidence of patient-reported adverse events, such as discomfort and blurred vision, was low and similar between the two groups (Dexamethasone Implant Group: 9.1%, Anti-VEGF Group: 13.0%, p=0.521). Additionally, the majority of patients in both groups reported improvement in daily activities (Dexamethasone Implant Group: 80.0%, Anti-VEGF Group: 75.9%, p=0.632), vision-related activities (Dexamethasone Implant Group: 70.9%, Anti-VEGF Group: 68.5%, p=0.782), and overall quality of life (Dexamethasone Implant Group: 78.2%, Anti-VEGF Group: 72.2%, p=0.492) (Table 4).

Table 4: Patient-reported outcomes for the Dexamethasone Implant Group and the Anti-VEGF Group

Patient-reported Outcome	Dexamethasone Implant Group (n=55)	Anti-VEGF Group (n=54)	p-value
	Frequency (%)/ Mean ± SD		
Treatment Satisfaction (Visual Function Questionnaire score)	78.6 ± 9.3	76.9 ± 8.7	0.328
Quality of Life (EQ-5D score)	0.78 ± 0.06	0.76 ± 0.07	0.215
Patient-reported Adverse Events (discomfort, blurred vision)	5 (9.1%)	7 (13.0%)	0.521
Patient-reported Improvement in Daily Activities	44 (80.0%)	41 (75.9%)	0.632
Patient-reported Improvement in Vision-related Activities	39 (70.9%)	37 (68.5%)	0.782
Patient-reported Improvement in Overall Quality of Life	43 (78.2%)	39 (72.2%)	0.492

Discussion

In this study, we compared the efficacy and safety of dexamethasone implant and anti-VEGF agents in the treatment of naive diabetic macular edema (DME). Our findings revealed similar improvements in visual and anatomical outcomes between the two treatment modalities over a 12-month follow-up period. However, notable differences were observed in the frequency of injections and the need for rescue therapy, suggesting potential implications for treatment selection and patient management.

The primary outcome of our study, change in best-corrected visual acuity (BCVA) from baseline, demonstrated no significant difference between the dexamethasone implant group and the anti-VEGF group at any time point. This finding is consistent with previous studies by Aksoy et al., Bolubasi et al., Maturi et al., and Limon et al., which have reported comparable visual outcomes between dexamethasone implant and anti-VEGF treatments in DME patients [13,14,15,16]. The absence of a significant difference in BCVA improvement suggests that both treatment modalities effectively restore visual function in naive DME patients.

Similarly, the change in central macular thickness (CMT) from baseline, a key anatomical parameter reflecting macular edema severity, did not differ significantly between the two groups throughout the study period. This aligns with previous studies by Comet et al., Aydin et al., and Busch et al., indicating similar reductions in CMT with dexamethasone implant and anti-VEGF therapies [17,18,19]. The observed anatomical improvements underscore the efficacy of both treatment options in resolving macular edema and restoring retinal morphology in DME patients.

Despite comparable efficacy in visual and anatomical outcomes, our study revealed significant differences in treatment burden between the dexamethasone implant and anti-VEGF groups. Patients in the dexamethasone implant group received fewer injections over the 12-month period compared to those in the anti-VEGF group, reflecting the sustained-release nature of the dexamethasone implant formulation. This finding is consistent with previous studies by Sever et al., Podkowin et al., Routier et al., and Callanan et al., demonstrating the extended treatment intervals and reduced injection frequency associated with dexamethasone implant therapy [20,21,22,23]. The lower treatment burden associated with dexamethasone implant may offer advantages in terms of patient convenience, compliance, and healthcare resource utilization.

Furthermore, the proportion of patients requiring rescue therapy was significantly lower in the dexamethasone implant group compared to the anti-VEGF group. This suggests that dexamethasone implant therapy may provide more durable and sustained treatment effects, reducing the need for additional interventions to manage persistent or recurrent DME. This finding is supported by evidence from studies by Lin et al., and Ceravolo et al., indicating a lower incidence of treatment-resistant DME and recurrence with dexamethasone implant therapy [24,25].

In terms of safety outcomes, both treatment modalities demonstrated favorable tolerability profiles with low rates of adverse events. The incidence of cataract progression, elevated intraocular pressure (IOP), and other ocular complications did not differ significantly between the two groups. This is consistent with previous literature suggesting comparable safety profiles for dexamethasone implant and anti-VEGF treatments in DME patients [21,23]. Notably, the incidence of endophthalmitis was low in both groups, further supporting the safety of intravitreal injections in real-world practice.

Conclusion

Overall, our study contributes to the growing body of evidence supporting the efficacy and safety of dexamethasone implant and anti-VEGF therapies in the management of naive DME. The findings highlight the importance of considering treatment burden, durability of response, and individual patient factors when selecting the optimal treatment approach for DME patients. Future studies incorporating long-term follow-up and cost-effectiveness analyses are warranted to further elucidate the comparative benefits and limitations of these treatment modalities in real-world clinical practice.

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