

Role of Combining Suprachoroidal Triamcinolone with Intravitreal Bevacizumab on Refractory Diabetic Macular Edema

PJO – Official Journal of
Ophthalmological Society of Pakistan



This work is licensed under a Creative Commons Attribution-Non-Commercial 4.0 International License.

Muhammad Irfan Karamat¹, Munib- ur-Rehman², Andleeb Zahare³,
Gul E Lala⁴, Nashrah Imtiaz⁵
^{1,2,4,5}*Ibrahim Eye Center, Lahore, ³Allama Iqbal Medical college, Lahore*

ABSTRACT

Purpose: To evaluate the effectiveness and safety of combination therapy using suprachoroidal triamcinolone acetonide (TA) and intravitreal bevacizumab in patients with refractory diabetic macular edema (DME).

Study Design: Interventional case series.

Place and Duration of Study: Ibrahim Eye Center, from December 2024 to September 2025.

Methods: This interventional case series included ten eyes with refractory DME that remained unresponsive despite receiving at least three previous intravitreal anti-VEGF injections. All patients received a single session of combination therapy consisting of intravitreal bevacizumab (1.25 mg/0.05 mL) and suprachoroidal triamcinolone acetonide (4 mg/0.1 mL). Central subfield thickness (CST) was measured using optical coherence tomography (OCT) at baseline and eight weeks after treatment. Changes in CST and treatment-related adverse events were evaluated.

Results: There were 5 males and 5 females, all with uncontrolled type II diabetes mellitus (HbA1c >6.5%). The duration of diabetes ranged from 12 to 17 years, with a mean of 14.3 ± 2.7 years. Mean CST decreased significantly from 667.5 ± 150 μ m at baseline to 363.4 ± 150.22 μ m at eight weeks following treatment ($p = 0.006$). Eight eyes (80%) achieved a reduction in CST of at least 50 μ m. No serious ocular or systemic adverse events were observed. A transient rise in intraocular pressure occurred in two patients and was successfully controlled with topical anti-glaucoma medication.

Conclusion: Combination therapy with suprachoroidal triamcinolone acetonide and intravitreal bevacizumab produced significant anatomical improvement in refractory DME with a favorable safety profile.

Keywords: Macular edema, Intravitreal, injection, Triamcinolone Acetonide, Bevacizumab, OCT.

How to Cite this Article: Karamat MI, Rehman MUR, Zahare A, Lala GE, Imtiaz N. Role of Combining Suprachoroidal Triamcinolone with Intravitreal Bevacizumab on Refractory Diabetic Macular Edema. 2026;42(4):373-378. Doi:10.36351/pjo.v42i4.2244

Correspondence: Gul E Lala
Ibrahim Eye Center, Lahore
Email: gula.lala2000@gmail.com

Received: September 30, 2025
Revised: August 1, 2026
Accepted: September 13, 2026

INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of vision loss and is broadly classified into non-proliferative

diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).¹ NPDR is characterized by the loss of pericytes, formation of microaneurysms, and increased vascular permeability resulting in retinal vascular leakage. In contrast, PDR develops due to retinal ischemia-induced imbalance between angiogenic and anti-angiogenic factors, leading to pathological neovascularization. Advanced PDR may result in vitreous hemorrhage and tractional retinal detachment. Both diabetic macular edema (DME) and PDR are major causes of visual impairment in advanced diabetic eye disease.²

DME is the leading cause of vision loss among patients with diabetes. Its prevalence ranges from 4.2% to 14.3% in individuals with type 1 diabetes mellitus (T1DM) and from 1.4% to 5.57% in those with type 2 diabetes mellitus (T2DM).³ Major risk factors for DME include poor glycemic control, dyslipidemia, hypertriglyceridemia, hypertension, pregnancy, and advanced diabetic nephropathy.⁴ Current treatment modalities include intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents, corticosteroids, laser photocoagulation, combination therapy with anti-VEGF and laser, and pars plana vitrectomy.⁵

Bevacizumab (Avastin) is a full-length monoclonal antibody that inhibits vascular endothelial growth factor (VEGF) and is widely used as an anti-angiogenic agent in the management of DME.⁶ Although DR cannot be cured, repeated intravitreal bevacizumab injections are administered at monthly or regular intervals until macular edema resolves or stabilizes. Seo et al,⁷ reported that monthly bevacizumab injections for at least three months may be required to achieve favorable anatomical outcomes. However, its long-term efficacy in maintaining visual acuity remains uncertain, and a subset of patients continue to exhibit persistent macular edema and progressive visual deterioration despite multiple intravitreal bevacizumab injections.

Triamcinolone acetonide (TA), in contrast, is a potent corticosteroid that suppresses inflammation through activation of lipocortin, thereby inhibiting phospholipase A2 and reducing the production of inflammatory mediators. TA is commonly used to control postoperative inflammation and treat ocular conditions such as corneal injury, allergic conjunctivitis, and uveitis. Potential adverse effects include cataract formation, steroid-induced glaucoma, and an increased risk of ocular infections.⁸ While bevacizumab primarily targets retinal angiogenesis, TA addresses the inflammatory component of DME. Consequently, combining these agents may provide synergistic therapeutic benefits in patients with refractory DME.

Although intravitreal TA has demonstrated efficacy in refractory DME, its use is frequently limited by steroid-induced elevation of intraocular pressure (IOP). In contrast, suprachoroidal administration of TA has shown comparable efficacy while minimizing the risk of IOP elevation.⁹ The suprachoroidal space, located between the sclera and

choroid, provides a targeted route for posterior segment drug delivery.¹⁰ Although intravitreal injection remains the standard route for treating retinal diseases, the suprachoroidal approach offers several potential advantages. Thomas et al,¹¹ successfully treated uveitic macular edema using a suprachoroidal injectable corticosteroid suspension. Because drug delivery through the suprachoroidal space achieves higher posterior segment concentrations with minimal exposure to the anterior segment, it is associated with a lower risk of steroid-induced glaucoma and cataract formation.¹² These characteristics make suprachoroidal TA a promising therapeutic option for patients with treatment-resistant DME while reducing steroid-related adverse effects.

The present study aimed to evaluate the efficacy and safety of combined suprachoroidal triamcinolone acetonide and intravitreal bevacizumab in patients with refractory DME who had shown an inadequate response to previous intravitreal bevacizumab therapy.

METHODS

This interventional case series included 10 eyes of 10 patients with refractory DME. Refractory DME was defined as persistent macular edema despite receiving at least three prior intravitreal bevacizumab injections. The study was approved by the Institutional review board/Ethical review board (**OSP-IRB/006-2025**).

Informed consent was taken. All patients underwent a comprehensive ophthalmic evaluation, including detailed medical history, refraction, and external ocular examination to exclude active infection. IOP was measured using a Goldmann applanation tonometer. Following pharmacological pupil dilation, fundus examination was performed using a Haag-Streit slit lamp biomicroscope with a Volk 90D lens. OCT was performed using the Nidek RS-3000 Retina Scan (Nidek Co., Ltd., Japan) to assess DME and measure central subfield thickness (CST) in micrometers (μm).

The procedure, along with its potential risks and complications including conjunctival congestion, subconjunctival hemorrhage, ocular pain, elevated IOP, and endophthalmitis was explained to all participants. Written informed consent was obtained from every patient before enrollment.

The inclusion criteria were age >18 years, uncontrolled type 2 diabetes mellitus, clear ocular media, adequate pupillary dilatation, normal baseline

IOP, and a CST of ≥ 275 μm . Exclusion criteria included central corneal opacity, visually significant cataract, vitreous hemorrhage, retinal detachment, uncontrolled glaucoma, previous pars plana vitrectomy, or any retinal pathology other than diabetic retinopathy that could influence macular edema during the study period. Pregnant or breastfeeding women, patients with a known hypersensitivity to the study medications, and uncooperative individuals were also excluded.

All procedures were performed in a sterile operating theatre by the same experienced ophthalmologist to minimize procedural variability. After confirming and marking the injection sites, topical anesthesia was achieved with 0.5% proparacaine hydrochloride. An anterior chamber paracentesis was performed by removing approximately 0.1 mL of aqueous humor. Intravitreal bevacizumab (1.25 mg/0.05 mL) was then injected using a sterile 27-gauge needle through the inferotemporal quadrant, 3.5 mm posterior to the limbus.

Following the intravitreal injection, 4 mg/0.1 mL of triamcinolone acetonide suspension was administered into the suprachoroidal space using a sterile 30-gauge needle inserted perpendicular to the scleral surface through the superotemporal quadrant, 3.5 mm posterior to the limbus. Gentle pressure was applied to the injection site using a sterile cotton-tipped applicator after needle withdrawal.

Patients were followed for eight weeks after treatment. The primary outcome measure was the change in CST measured by OCT. Treatment was considered anatomically effective if the CST decreased by ≥ 50 μm from baseline at the eight-week follow-up. Secondary outcomes included the occurrence of ocular or systemic adverse events, particularly elevation of IOP.

RESULTS

The study included ten patients (10 eyes), comprising five males and five females. All participants had uncontrolled type 2 diabetes mellitus with an HbA1c level $>6.5\%$. The duration of diabetes ranged from 12 to 17 years, with a mean duration of 14.3 years. The patients' age ranged from 51 to 65 years, with a mean age of 57.6 ± 8.57 years. Five eyes (50%) were phakic, while the remaining five (50%) were pseudophakic.

All patients had previously received five to seven intravitreal bevacizumab injections during the preceding six months without achieving a satisfactory anatomical response, thereby fulfilling the criteria for refractory diabetic macular edema.

The mean CST at baseline was 667.5 ± 157.8 μm (median: 630 μm). At the 8-week follow-up, the mean CST had significantly decreased to 363.4 ± 149.1 μm (median: 305 μm). The mean reduction in CST was 304.1 ± 266.5 μm , which was statistically significant ($p = 0.006$). Eight of the ten eyes (80%) achieved the predefined criterion for anatomical success, demonstrating a reduction in CST of at least 50 μm from baseline.

Although substantial anatomical improvement was observed, no statistically significant improvement in best-corrected visual acuity was detected during the 8-week follow-up period.

Baseline IOP was within the normal range in all patients. A transient elevation in IOP occurred in two patients during the first two weeks following treatment and was successfully controlled with topical anti-glaucoma medication. No serious ocular or systemic adverse events, including endophthalmitis, retinal detachment, vitreous hemorrhage, or drug-related systemic complications, were observed during the study period.

Table1: Pre-and Post-Injection change in the Central Subfield Thickness

Age (years)	Duration of Diabetes (years)	Number of Injections	Pre-Injection (Macular Thickness) (um)	Post- Injection Macular Thickness (um)
51	15	6	825	270
62	13	7	845	228
59	17	5	810	226
54	12	7	855	210
61	16	6	600	610
60	13	7	400	260
55	15	6	550	340
65	17	5	610	510
57	13	6	650	440
52	12	5	530	540

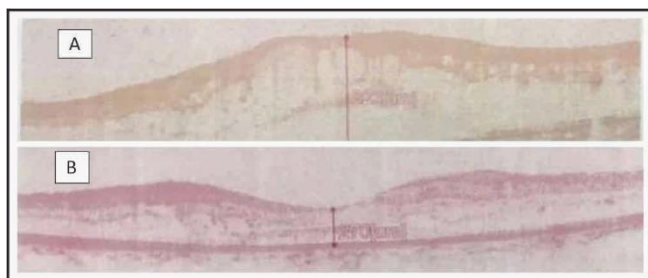


Figure 1: Changes in CST recorded by OCT. (A) Baseline CST documented as 823µm before treatment (B) CST reduced to 270µm 8 weeks after treatment.

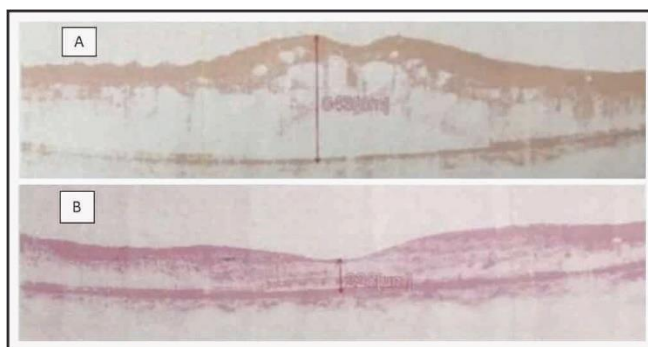


Figure 2: Changes in CST recorded by OCT. (A) Baseline CST documented as 843µm before treatment (B) CST reduced to 228µm 8 weeks after treatment.

DISCUSSION

The findings of the present study demonstrated a statistically significant reduction in CST following combination therapy with intravitreal bevacizumab and suprachoroidal TA in patients with refractory DME. However, despite the marked anatomical improvement, no significant improvement in visual acuity was observed during the 8-weeks follow-up period. This may be attributed to the chronic nature of refractory DME, where longstanding structural damage to the macula can limit functional recovery despite successful resolution of retinal edema.

Our findings are consistent with those of Jeon et al.,¹³ who reported only limited benefit from six consecutive monthly intravitreal bevacizumab injections in patients with DME, suggesting that anti-VEGF monotherapy may be insufficient in refractory cases. In contrast, other investigators have demonstrated improved visual outcomes with combination therapy or repeated anti-VEGF administration. Tsilimbaris et al.,⁴ evaluated 17 patients treated with a combination of intravitreal triamcinolone acetonide and bevacizumab and

reported significant improvement in BCVA, with mean visual acuity improving from 1.08 ± 0.56 log MAR at baseline to 0.77 ± 0.56 log MAR over a 6-month follow-up period. Similarly, another study demonstrated that three consecutive monthly intravitreal anti-VEGF injections resulted in significant reductions in central macular thickness accompanied by improvements in BCVA.¹⁵

The discrepancy between our findings and previous reports regarding visual acuity may be explained by differences in disease chronicity, baseline retinal damage, duration of follow-up, and route of corticosteroid administration. While our study demonstrated encouraging short-term anatomical outcomes, a longer follow-up period may be necessary to determine whether these anatomical improvements translate into meaningful visual recovery. The suprachoroidal route has emerged as a minimally invasive drug delivery approach that achieves high drug concentrations in the posterior segment while minimizing exposure to the anterior segment, thereby reducing the risk of steroid-related adverse effects. The HULK trial evaluated the efficacy of suprachoroidal TA, administered alone or in combination with intravitreal aflibercept, in patients with refractory DME.¹⁶ The investigators concluded that suprachoroidal TA was safe, well tolerated, and effective, with repeated injections producing significant reductions in CST. These findings are consistent with our results, which also demonstrated marked anatomical improvement following suprachoroidal corticosteroid therapy.

Similarly, Tabl et al.,¹⁷ compared intravitreal and suprachoroidal TA in patients with refractory DME associated with epiretinal membrane. Patients received a single TA injection through either the intravitreal or suprachoroidal route. The authors reported significantly greater IOP elevation in the intravitreal group, whereas the suprachoroidal group demonstrated significant improvements in BCVA and reductions in CST at three months. These findings further support the safety advantage of the suprachoroidal route while maintaining therapeutic efficacy.

Thomas et al.,¹¹ also demonstrated the effectiveness of suprachoroidal corticosteroid therapy in patients with noninfectious uveitis, with or without associated macular edema. Following two suprachoroidal injections, most patients experienced a reduction in retinal inflammation and macular edema on optical coherence tomography, accompanied by

improvements in BCVA at all post-baseline visits. Although the underlying disease differs from DME, these findings reinforce the ability of the suprachoroidal route to deliver corticosteroids effectively to the posterior segment.

The efficacy of suprachoroidal TA as a standalone treatment for refractory DME has also been demonstrated by Tayyab et al,¹⁸ In their interventional study involving 24 patients, the mean CST decreased from $636.5 \pm 200.11 \mu\text{m}$ at baseline to $304.54 \pm 67.43 \mu\text{m}$ and $302.66 \pm 66.93 \mu\text{m}$ at one and three months, respectively. Significant improvements were also observed in BCVA without clinically important increases in IOP. These findings, together with those of the present study, highlight the potential of the suprachoroidal route as an effective treatment strategy for refractory DME while potentially reducing the frequency of clinic visits and intravitreal injections.

Although both intravitreal and suprachoroidal corticosteroid injections have demonstrated efficacy in the management of refractory DME, the principal advantage of the suprachoroidal route appears to be its superior safety profile. Shaikh et al,¹⁹ reported that IOP remained stable following suprachoroidal TA administration, supporting the concept that targeted posterior segment drug delivery minimizes corticosteroid exposure to the anterior segment and reduces the risk of steroid-induced glaucoma.

The encouraging anatomical outcomes observed in our study suggest that combining intravitreal bevacizumab with suprachoroidal TA may provide additive therapeutic benefits by targeting both the angiogenic and inflammatory pathways involved in DME. However, evidence regarding combination therapy remains limited. Ciulla et al,²⁰ in a retrospective chart review, reported significant improvements in both BCVA and CST among patients treated with intravitreal ranibizumab after previous therapies including intravitreal TA, bevacizumab, and laser photocoagulation, underscoring the potential value of multimodal treatment strategies in refractory disease.

The present study has several limitations. The small sample size and relatively short follow-up period limit the generalizability of the findings and preclude assessment of long-term efficacy and safety. Furthermore, the absence of a control group prevents direct comparison with monotherapy. Larger randomized controlled trials with longer follow-up are

warranted to confirm the efficacy, durability, and safety of combined intravitreal bevacizumab and suprachoroidal triamcinolone acetonide in the management of refractory diabetic macular edema.

CONCLUSION

Combination therapy with intravitreal bevacizumab and suprachoroidal TA resulted in significant anatomical improvement in patients with refractory diabetic macular edema, as demonstrated by a substantial reduction in CST. Although no significant improvement in visual acuity was observed during the short follow-up period, the treatment was well tolerated, with no serious ocular or systemic adverse events.

Funding: This study was not funded by any organization.

Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board (OSP-IRB/006-2025)

REFERENCES

1. Chong DD, Das N, Singh RP. Diabetic retinopathy: Screening, prevention, and treatment. *Cleve Clin J Med*. 2024;**91**(8):503-510. Doi: 10.3949/ccjm.91a.24028
2. Li H, Liu X, Zhong H, Fang J, Li X, Shi R, et al. Research progress on the pathogenesis of diabetic retinopathy. *BMC Ophthalmol*. 2023;**23**(1):372. Doi: 10.1186/s12886-023-03118-6
3. Zhang J, Zhang J, Zhang C, Zhang J, Gu L, Luo D, et al. Diabetic macular edema: current understanding, molecular mechanisms and therapeutic implications. *Cells*. 2022;**11**(21):3362. Doi: 10.3390/cells11213362
4. Gonzalez-Cortes JH, Martinez-Pacheco VA, Gonzalez-Cantu JE, Bilgic A, de Ribot FM, Sudhalkar A, et al. Current treatments and innovations in diabetic retinopathy and diabetic macular edema. *Pharmaceutics*. 2022;**15**(1):122. Doi: 10.3390/pharmaceutics15010122.
5. Tatsumi T. Current treatments for diabetic macular edema. *Int J Mol Sci*. 2023;**24**(11):9591. Doi: 10.3390/ijms24119591
6. Grisanti S, Ziemssen F. Bevacizumab: off-label use in ophthalmology. *Indian J Ophthalmol*. 2007;**55**(6):417-420. Doi: 10.4103/0301-4738.36474

7. **Seo JW, Park IW.** Intravitreal bevacizumab for treatment of diabetic macular edema. *Korean J Ophthalmol.* 2009;**23(1)**:17-22. Doi: 10.3341/kjo.2009.23.1.17
8. **Reichle ML.** Complications of intravitreal steroid injections. *Optometry.* 2005;**76(8)**:450-460. Doi: 10.1016/j.optm.2005.06.013
9. **Shahid MH, Rashid FA, Tauqeer SA, Ali RA, Farooq MT, Aleem NO.** Comparison of suprachoroidal triamcinolone injection with intravitreal bevacizumab vs intravitreal bevacizumab only in treatment of refractory diabetic macular edema. *Pak. J. Med. Health Sci.* 2022;**16**:301. Doi:10.53350/pjmhs22166301
10. **Chiang B, Jung JH, Prausnitz MR.** The suprachoroidal space as a route of administration to the posterior segment of the eye. *Adv. Drug Deliv. Rev.* 2018;**126**:58-66. Doi: 10.1016/j.addr.2018.03.001
11. **Thomas J, Kim L, Albini T, Yeh S.** Triamcinolone acetonide injectable suspension for suprachoroidal use in the treatment of macular edema associated with uveitis. *Expert Rev Ophthalmol.* 2022;**17(3)**:165-173. Doi: 10.1080/17469899.2022.2114456
12. **Zakaria YG, Salman AG, Said AM, Abdelatif MK.** Suprachoroidal versus intravitreal triamcinolone acetonide for the treatment of diabetic macular edema. *Clin Ophthalmol.* 2022:733-746. Doi:10.2147/OPTH.S351853
13. **Jeon S, Lee WK.** Effect of intravitreal bevacizumab on diabetic macular edema with hard exudates. *Clin Ophthalmol.* 2014:1479-1486. Doi: 10.2147/OPTH.S66405
14. **Tsilimbaris MK, Pandeledonidis V, Panagiotoglou T, Arvanitaki V, Fragiskou S, Eleftheriadou M, et al.** Intravitreal combination of triamcinolone acetonide and bevacizumab (Kenacort-Avastin) in diffuse diabetic macular edema. *Semin Ophthalmol.* 2009;**24(6)**:225-230. Doi: 10.3109/08820530903389775
15. **Ahmadieh H, Ramezani A, Shoeibi N, Bijanzadeh B, Tabatabaei A, Azarmina M, et al.** Intravitreal bevacizumab with or without triamcinolone for refractory diabetic macular edema; a placebo-controlled, randomized clinical trial. *Graefes Arch Clin Exp Ophthalmol.* 2008;**246**:483-489. Doi: 10.1007/s00417-007-0688-0.
16. **Wykoff CC, Khurana RN, Lampen SI, Noronha G, Brown DM, Ou WC, et al.** Suprachoroidal triamcinolone acetonide for diabetic macular edema: The HULK trial. *Ophthalmol Retina.* 2018;**2(8)**:874-877. Doi: 10.1016/j.oret.2018.03.008.
17. **Tabl AA, Soliman TT, Elsayed MA, Tabl MA.** A randomized trial comparing suprachoroidal and intravitreal injection of triamcinolone acetonide in refractory diabetic macular edema due to epiretinal membrane. *J Ophthalmol.* 2022;2022. Doi: 10.1155/2022/7947710.
18. **Tayyab H, Ahmed CN, Sadiq MA.** Efficacy and safety of suprachoroidal triamcinolone acetonide in cases of resistant diabetic macular edema. *Pak J Med Sci.* 2020;**36(2)**:42. Doi: 10.12669/pjms.36.2.1194
19. **Shaikh K, Ahmed N, Kazi U, Zia A, Aziz MZ.** Comparison between suprachoroidal triamcinolone and intravitreal triamcinolone acetonide in patients of resistant diabetic macular edema. *Pak J Ophthalmol.* 2023;**39(1)**. Doi: 10.36351/pjo.v39i1.1480
20. **Ciulla TA, Hussain RM, Ciulla LM, Sink B, Harris A.** Ranibizumab for diabetic macular edema refractory to multiple prior treatments. *Retina.* 2016;**36(7)**:1292-1297. Doi: 10.1097/IAE.0000000000000876

Authors Designation and Contribution

Muhammad Irfan Karamat; *Medical Director: Concepts, Design.*

Munib Ur Rehman; *Consultant Ophthalmologist: Design*

Andleeb Zahare; *Assistant Professor: Manuscript Editing.*

Gul E Lala; *Optometrist: Literature Search, Manuscript Review.*

Nashrah Imtiaz; *Optometrist: Literature Search, Data Acquisition, Data Analysis, Statistical Analysis.*

