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Combination treatment strategies for diabetic macular edema: a systematic review and meta analysis

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ABSTRACT

Introduction: Diabetic macular edema (DME) is a leading cause of vision loss in patients with diabetes. This meta-analysis compares the efficacy and safety of combination therapy and anti-VEGF monotherapy for DME treatment.

Method: A systematic literature search was conducted from January 2010 to December 2024, scanning through PubMed, Scopus, and Proquest databases. Trials comparing combination therapy and monotherapy in DME patients were included. This review adhered to PRISMA guidelines and risk of bias was assessed using Rob2 and ROBINS-I tools. Efficacy and safety were analyzed using standardized mean differences (SMD) and pooled in a forest plot using RevMan. PROSPERO registered (CRD420251028671)

Result: 12 RCTs and 1 non-randomized study involving 923 eyes. Combination therapy significantly reduces central macular thickness (CMT) compared to anti-VEGF monotherapy (SMD 0.49; 95% CI, 0.18-0.81; P <0.05; I^2 = 76%). Combination therapy showed a greater proportion of Best Corrected Visual Acuity (BCVA) reduction, although the difference was not statistically significant (SMD, 0.83; 95% CI, -0.03-1.70; P = 0.06; I^2 = 96%). Subgroup analysis indicated laser and anti-VEGF was effective combination in reducing CMT (SMD, 0.74; 95% CI, 0.18-0.81; P <0.05; I^2 = 83%). Diclofenac and Anti-VEGF also effective combination in reducing mean BCVA (SMD, 0.62; 95% CI, 0.25-0.99; P <0.05; I^2 = 0%). IOP elevation is reported in combination therapy includes corticosteroid.

Conclusion: Combination therapies (Laser or Diclofenac plus anti-VEGF) show superior efficacy in improving BCVA and reducing CMT in DME patients compared with monotherapy, with tolerable adverse events.

Keywords: Diabetic Macular Edema, Anti-VEGF Therapy, Central Macular Thickness, Best Corrected Visual Acuity.
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INTRODUCTION

Diabetic retinopathy is a common complication of diabetes that often leads to vision impairment and blindness, primarily due to diabetic macular edema.[1] It remains a leading cause of vision impairment among working-age adults, driven by microvascular leakage and chronic retinal inflammation that thicken the fovea and degrade photoreceptor function. Anti-vascular endothelial growth factor remains the first-line treatment for DME, though it requires frequent injections. Other approved treatments include laser photocoagulation, intravitreal corticosteroids, and anti-inflammatory agents.[2] Corticosteroids reduce inflammation and vascular leakage but may increase intraocular pressure and the risk of cataracts.[3]

Over the past decade, intravitreal anti-VEGF therapy has become the first-line standard for center-involved DME (CI-DME), delivering clinically meaningful visual gains and anatomical drying in the majority of patients[2]. Contemporary clinical guidance recommends initiating anti-VEGF in CI-DME with individualized retreatment based on visual and OCT response, while reserving focal/grid laser and corticosteroids for selected scenarios. This therapeutic landscape sets the stage for a rigorous appraisal of whether combination strategies can further improve outcomes or reduce treatment burden beyond anti-VEGF monotherapy. Laser therapy minimizes retinal damage while reducing leakage.[2] This meta-analysis evaluates whether combination therapy improves outcomes over anti-VEGF monotherapy for DME.

METHODS

Study Registration

This systematic review adhered to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[4] The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD420251028671.

Search Strategy and Eligibility Criteria

A systematic literature search was conducted using the electronic databases PubMed, Scopus, and ProQuest, covering studies published from January 2010 to December 2024. The search included randomized controlled trials (RCTs) and controlled clinical trials that compared combination therapy with monotherapy using anti-VEGF agents in patients with

diabetic macular edema (DME). The search was last conducted in March 2025. The following treatment terms were included in the search string strategy: Ranibizumab, Bevacizumab, Pegaptanib, Aflibercept, Vegf trap-eye, Steroid, Corticosteroid, Dexamethasone, Fluocinolone, Triamcinolone, anti-VEGF, anti-vascular endothelial growth factor, and Intravitreal Injection. These terms were combined with "Combination therapy" OR "Combined therapy" AND "Light Coagulation"[Mesh] OR "laser photocoagulation" AND ("Macular Edema"[Mesh] OR "Irvine-Gass syndrome" OR "cystoid macular dystrophy").

Studies were included if they involved patients of any age and sex diagnosed with type 1 or type 2 diabetes mellitus, presenting with treatment-naïve clinically significant diabetic macular edema that responded to intravitreal anti-VEGF therapy. Studies were excluded if they involved macular edema secondary to retinal vein occlusion or other causes, or patients with anti-VEGF-resistant DME. This review adhered to the PRISMA guidelines.

Study Selection and Data Collection

Titles and abstracts were screened by two independent reviewers, followed by full-text screening. Screening was carried out using Rayyan (an AI-powered tool for Systematic.Literature Reviews) based on the inclusion criteria outlined above. Any disagreements between reviewers were resolved through discussion. All data were compiled using Microsoft Excel.

The following baseline characteristic data were extracted: demographic data, methodological characteristics, characteristics of the subjects, and outcome data. The primary outcome was the final change in Best Corrected Visual Acuity (BCVA) at the final time point of intervention. Secondary outcomes included changes in retinal thickness and adverse events (AEs). The change in BCVA was reported in logMAR notation. If BCVA was presented in ETDRS letters, it was converted to logMAR notation.

Quality Assessment

The risk of bias for the included trials was assessed using the Cochrane Risk of Bias (RoB-2) tool for randomized trials and the ROBINS-I tool for nonrandomized studies. Seven domains were assessed: confounding, classification of intervention, selection into the study, deviations from intended intervention, missing data, measurement of the outcome, and selection of reported results. Two reviewers independently performed this assessment, and any disagreements were managed by discussion.

Statistical Analysis

The systematic review and meta-analysis were conducted according to the recommendations of the Cochrane Collaboration and PRISMA guidelines. For dichotomous outcomes, comparative effect sizes were calculated as odds ratios (ORs) with 95% confidence intervals (CIs) For continuous outcomes, the mean difference (MD) with 95% CI was reported using inverse-variance weighted meta-analysis. A random-effects model was applied to all outcomes.

Heterogeneity was assessed by examining forest plots to determine if the direction of effect was consistent across studies and whether the confidence intervals for individual study estimates overlapped. The I^2 statistic was also considered, with values greater than 50% indicating substantial inconsistency in the results, suggesting that a pooled result may not be informative. All statistical analyses were performed using Review Manager 5.4.1.

RESULTS

The initial retrieval obtained 1056 records in total, of which 227 duplicated references were eliminated. A total of 827 records were identified through a detailed

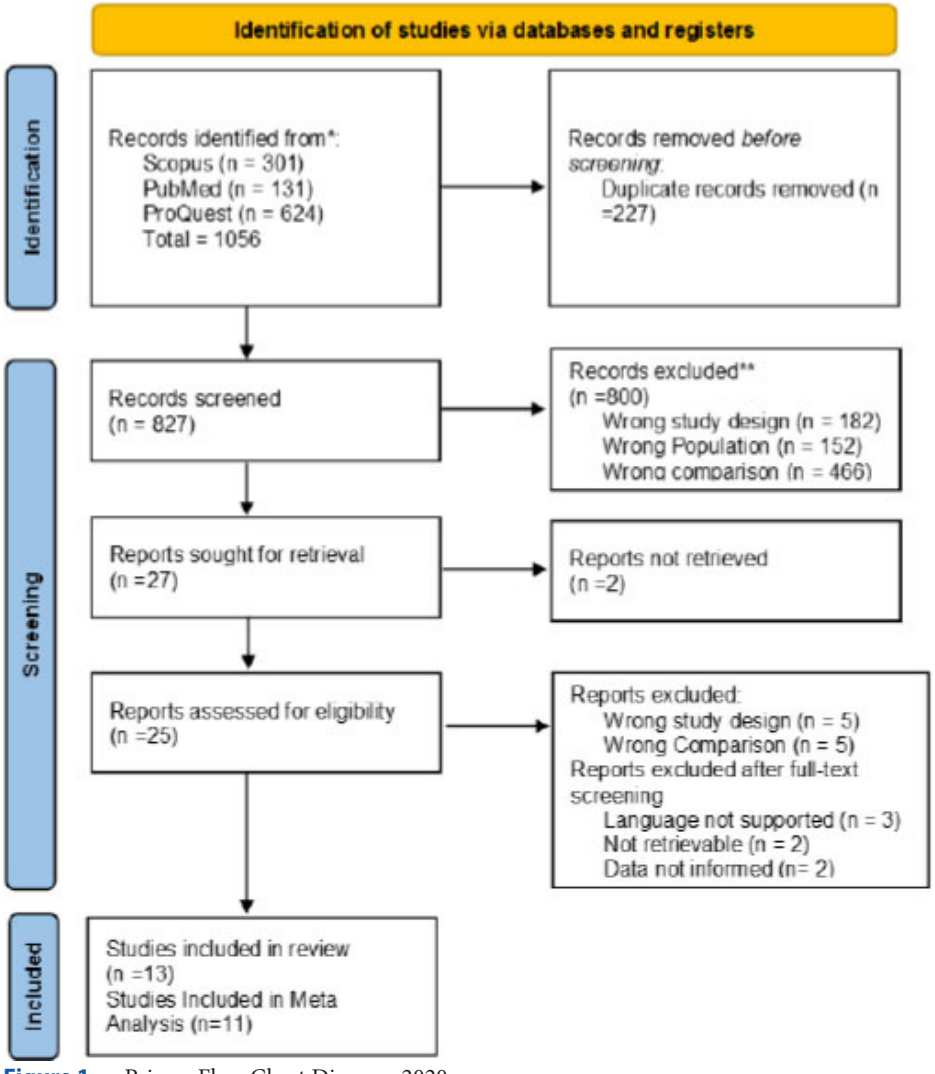

Figure 1. Prisma Flow Chart Diagram 2020.

screening of titles and abstracts. Twenty seven full-text articles were identified and sought for retrieval. Twentie five reports assessed for eligibility in the meta-analysis. Twelve article were excluded, after full screening 13 reports are included in the review. Eleven articles were included in the meta analysis and consisted of 12 RCT and one non randomized study.

In total, 923 eyes were in this systematic review. The primary outcomes (BCVA/CMT/adverse events) were recorded during follow-up visits ranging from 1 to 24 months. Eleven studies included in meta analysis for CMT reduction, and 10 studies included in meta analysis for BCVA change. Detailed information on all trials is summarized in Figure 2. The statistical meta-analysis was limited to BCVA and mean change of CMT because they're the only variables reported in all included studies.

Risk for bias for the included studies was assessed using the Cochrane Risk of Bias Tool 2. Figure 3 shows the outcomes of the Cochrane Risk of Bias Tool 2 evaluation. Two studies considered as high risk of bias for deviation from intended interventions and missing outcome data respectively for each study. Some concerns about the risk for bias were found for the randomization process in 2 studies (15%), for deviation from intended interventions in 5 studies (38%), for missing outcome data in 4 study (30%), for measurement of the outcomes and for selection of reported results both are considered low risk of bias. All remaining domains were evaluated as having a low risk for bias. One non-randomized study were assessed and graded using ROBINS-I and found to have a low risk of bias for all domain indicating an overall high quality.

Overall our study suggest that mean BCVA changes are not statistically significant with combination therapy (P=0.06 ;MD = 0.83, 95% CI [-0.03, 1.70]). For subgroup analysis have found that

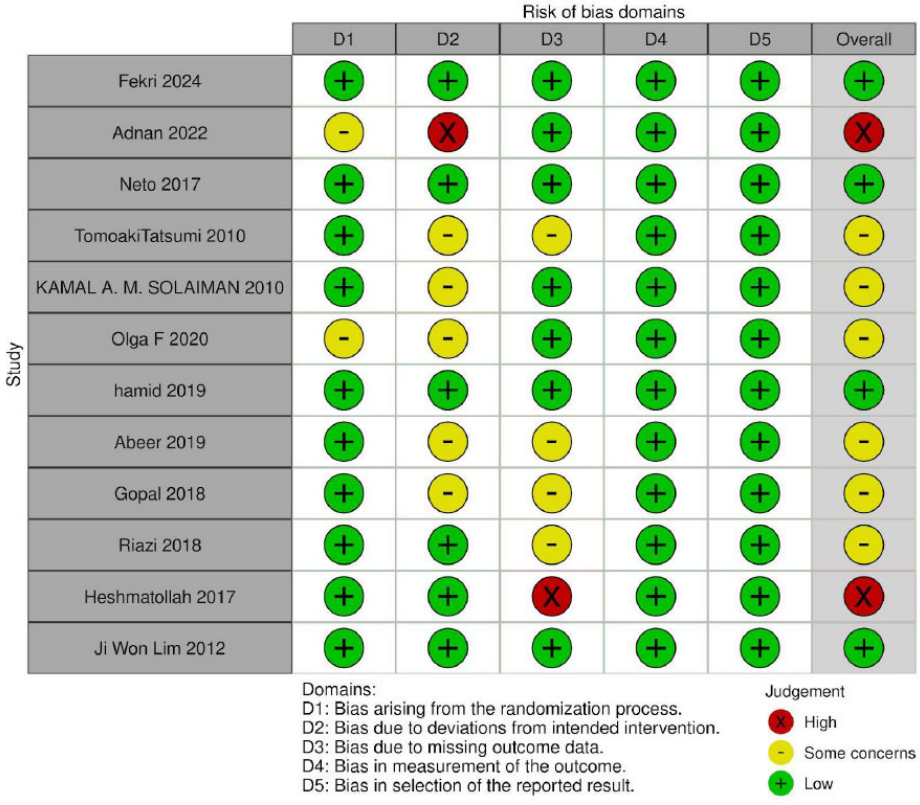

Figure 2. Risk of Bias.

Table 1. Characteristics of Study

Study ID	Study Design	Location	Disease	Treatment	Sample size (M/F)	Age (mean ± SD, years)	Eyes(N)	Follow-up	Outcomes
Fekri, 2024	RCT	Iran	DME	IV Bevacizumab (IVB) + timolol–dorzolamide	21/25	C: 60.43 ±7.67 M: 58.52±8.4	46	1 month	(1), (2), (3), (4)
Adnan Ahmad, 2022	RCT	Pakistan	Naive DME	IVB+ Diclofenac (IVD)	22/18	62.44±7.94	40	4, 12, 24 weeks	(1), (2), (3), (4)
A. O. Giyasova, 2023	Non-Randomized Trial	Uzbekistan	DME	IVB +SIMPLE (subthreshold Micropulse laser exposure)	34/48	M: 56.3±3.7 C :54.6±3.4	150	12 months	(1), (2)
Neto, H.O, 2017	RCT	Brazil	Non-ischemic DME	IVB + Intravitreal Triamcinolone (IVT)	61/50	Not Informed	111	6 months	(1), (2), (3), (4)
Tomoaki Tatsumi, 2022	RCT	Japan	DME	Intravitreal aflibercept (IVA) + Subthreshold Laser (SL)	27/22	C: 66.9 ± 9.4 M: 69.3 ± 7.4	51	48,96 weeks	(1), (2), (3), (4)
Solaiman, K.A.M., 2010	RCT	Egypt	Diffuse DME	IVB + Macular Photocoagulation (MPL)	35/27	M: 56 ± 43–72 C: 59 ± 47–68	62	1 day – 6 months	(1), (2)
Olga Furashova, 2020	RCT	Germany	Non-ischemic DME	IV Ranibizumab + Micropulse Diode Laser	14/5	70.74 ± 8.03	19	12 months	(1), (2), (3)
Hamid Ahmadieh, 2019	RCT	Iran	Severe DME	IVB+ Rho-kinase inhibitor	22/22	57.9±8.4	44	6 months	(1), (2)
Abeer M. Khattab, 2019	RCT	Kuwait	DME	IVA + MPL	32/22	M: 55.7 ± 3.4 C: 59.4 ± 4.3	54	18 months	(1), (2), (3)
Gopal K. Das, 2018	RCT	India	Diffuse DME	IVB + MPL	41/19	M: 54.63±8.34 C: 52.50±9.64	60	6 months	(1), (2), (3), (4)
Mohammad Riazi-Esfahani, 2018	RCT	Iran	Bilateral DME	IVB + IVT	21/25	62 ± 8.6, (46–81)	96	6 months	(1), (2), (3), (4)
Heshmatollah Ghanbari, 2017	RCT	Iran	Naive DME	IVD+IVB	40/40	M: 62.98 ± 8.182 C: 60.45 ± 8.056	80	1 month	(1), (2), (3), (4)
Ji Won Lim, 2012	RCT	Korea	DME	IVB + IVT	50/61	60.4 ± 7.4	110	12 months	(1), (2), (3)

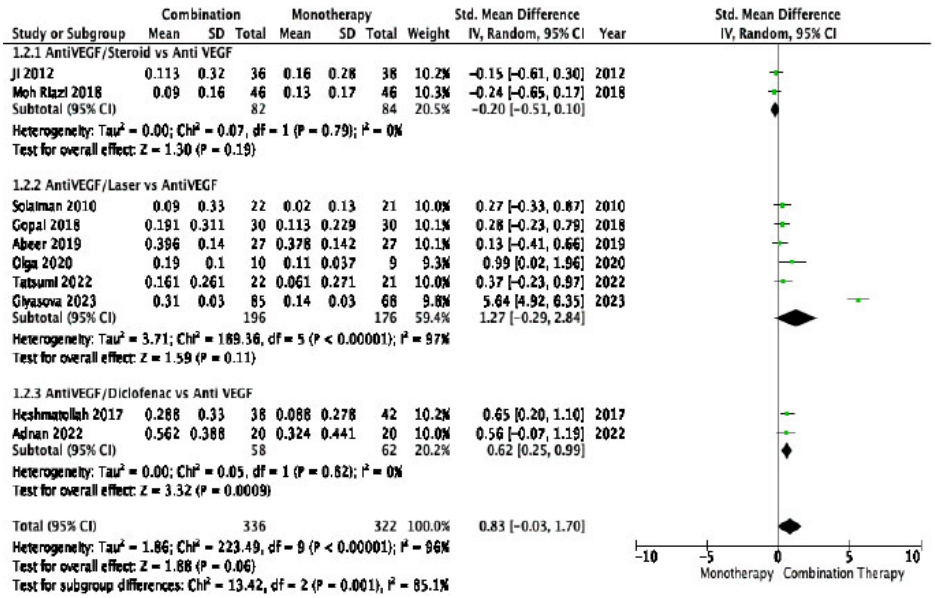

Figure 2. Forest-plot for Mean BCVA Changes. CI: Confidence interval.

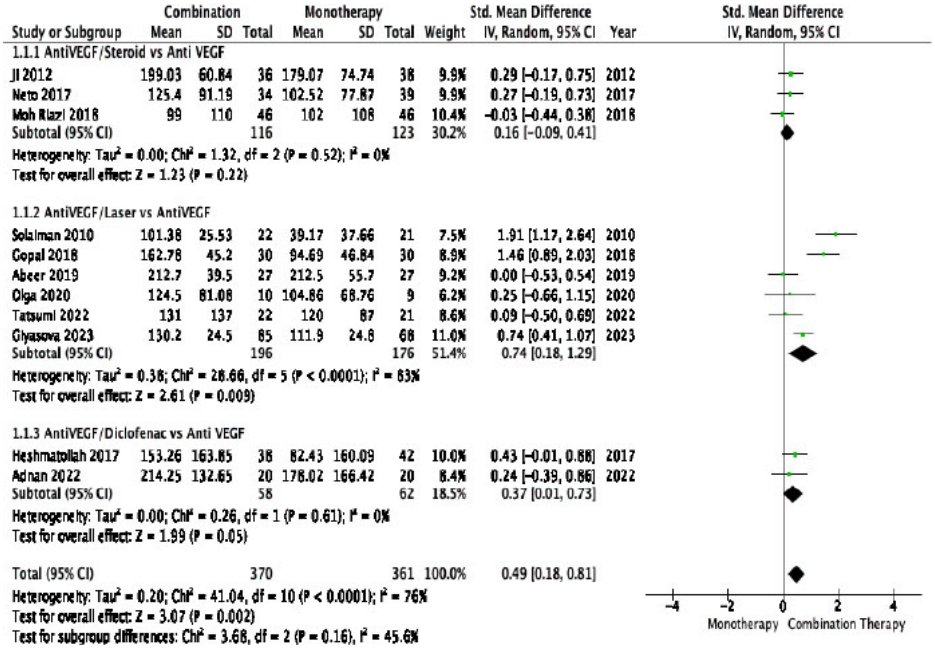

Figure 3. Forest-plot for Central Macular Thickness. CI: Confidence interval.

anti-VEGF and diclofenac are the most favoured combination therapy among others for BCVA changes. (MD = 0.62, 95% CI [0.25, 0.99]) and no heterogeneity was observed (I2 = 0%).

Overall our study suggest that CMT changes are statistically significant with combination therapy (P=0.02 ;MD = 0.49, 95% CI [0.18, 0.81]). Subgroup analysis have found that the overall mean difference of CMT changes improved statistically significantly with laser therapy (0.74 (95% CI [0.18,1.29]), Heterogeneity was detected (I2 = 83%).

Rho-Kinase Inhibitor and Anti-VEGF

Only one trial assesed the use of Rho-kinase Inhibitor with Anti-VEGF as combination therapy of DME treatment. Ahmadieh et al[5] showed at 6 months improvement of mean BCVA significantly higher in combination therapy than in the monotherapy group (p=0.008 and p<0.00), CMT reduction was significant in combination therapy(p<0.001) but not significant in monotherapy group compared with the baseline value (p>0.99).

Topical Timolol-Dorzolamide and Anti-VEGF

One study evaluated the use of topical timolol as adjunctive therapy to anti-VEGF to treat DME. Fekri et al[6] found after 1 month that the mean reduction in CMT was statistically signifcant in the combination therapy group (p-within<0.001). Mean BCVA in the combination therapy improved significantly (p-within=0.002). The intergroup diference analysis of BCVA changes was also not statistically signifcant (p=0.244).

Two trials showed elevated IOP after IVT injection, both study showed controlled IOP with glaucoma medication.[7,8] Neto et al[9] concluded the Bevacizumab Group shows a greater improvement in BCVA compared to the Combined Bevacizumab + Triamcinolone Group.

DISCUSSION

Current treatments for diabetic macular edema (DME) face several limitations, including the high costs, repeated injections, and prolonged treatment cycles associated with anti-VEGF therapy, which burden both patients and healthcare providers. Intravitreal corticosteroid injections (IVT) are constrained by the risk of elevated intraocular pressure and cataract formation, while laser photocoagulation, once a first-line option, is now considered an adjunctive therapy.[10] A recent study demonstrated significant reductions in central macular thickness (CMT) with combination therapy, particularly in the laser and diclofenac subgroup, providing potential guidance on when to employ such treatments. Current consensus guidelines recommend switching from anti-VEGF therapy if the eye shows less than 20% reduction in central retinal thickness and gains fewer than five letters after three to six injections.[11]

Combining anti-VEGF agents with corticosteroids may represent a promising strategy to enhance the therapeutic outcomes in DME management.[12–14] Our

study found that combination therapy was comparable with monotherapy in reducing central macular thickness (CMT). In contrast, Grad et al[15] (n=1166 eyes) reported that the reduction in retinal thickness at 24-month follow-up was significantly greater with combination therapy than with anti-VEGF monotherapy. However, regarding improvements in best-corrected visual acuity (BCVA). Zhou et al[16] (n=1436 eyes) also observed that the combination of corticosteroids with anti-VEGF agents did not result in improvement BCVA outcomes compared to anti-VEGF monotherapy. Nevertheless, corticosteroid use is associated with adverse events such as cataract formation and elevated intraocular pressure (IOP).[16]

Our study suggests that combination therapy with LASER and anti-VEGF injections showed a greater mean reduction in central macular thickness (CMT), consistent with findings from Meng et al[17] who reported superior central retinal thickness (CRT) recovery with conbercept combined with retinal laser photocoagulation, and Huang et al[18] who found intravitreal conbercept combined with panretinal photocoagulation (PRP) more effective for visual recovery than PRP monotherapy. LASER Techniques like focal/grid laser and subthreshold MicroPulse Laser Therapy (MPLT) may stabilize retinal structures, reduce pro-inflammatory cytokines, and enhance anti-VEGF efficacy while potentially decreasing injection frequency. Several studies including DRCR.net Protocol I[19], READ-2[20], and RESTORE[20] have shown that combining laser photocoagulation with anti-VEGF treatments improves visual outcomes and reduces injection frequency. However, variations in study design and sample characteristics warrant further trials to determine the optimal timing for LASER addition to anti-VEGF treatment to maximize visual outcomes.

Non-steroidal anti-inflammatory drugs (NSAIDs), such as topical diclofenac sodium, have shown potential in treating diabetic macular edema (DME) by inhibiting prostaglandin biosynthesis and reducing inflammation. In our study, combination therapy with anti-VEGF agents and diclofenac sodium resulted in a reduction of central macular thickness (CMT) with no statistically significant when compared to anti-VEGF monotherapy. Similarly, Sandra et al[21] reported a reduction in CMT with combination therapy, but without statistical significance. However, Hesmatollah et al[22] observed a significantly greater reduction in CMT with combination therapy, suggesting variability in treatment responses. In terms of best-corrected visual acuity (BCVA), our study demonstrated a statistically significant improvement with the combination therapy. This finding aligns with studies by Supanji et al[23] and Hesmatollah et al[22] which also reported significant improvements in patients treated with both anti-VEGF agents and diclofenac sodium. Importantly, no adverse events were reported in our study.

Topical timolol–dorzolamide may serve as a potential adjuvant therapy when combined with anti-VEGF treatment. Sridhar et al[24] found in cases of neovascular age-related macular degeneration (AMD) with persistent exudation, anti-VEGF therapy led to a significant reduction in central macular thickness (CMT) and subretinal fluid. Dorzolamide may affect Muller cells and retinal pigment epithelial pump function to regress retinal fluid, decrease edema and increase retinal and choroidal blood flow.[25] Our study found one study evaluated intravitreal Bevacizumab with topical 2% / 0.5% 5 mL timolol–dorzolamide eye drop resulted in a statistically significant reduction in CMT and improvement in best-corrected visual acuity (BCVA). Similarly, Mirshahi et al[26] observed greater reductions in CMT and improvements in BCVA in eyes treated with both IVB and timolol–dorzolamide. No adverse events were observed in our study.

Combination therapy with rho kinase inhibitors and anti-VEGF has shown improved mean BCVA and reduced CMT compared to monotherapy, highlighting the potential of rho kinase inhibitors in treating diabetic macular edema (DME), especially in patients refractory to conventional anti-VEGF therapies. Fasudil, ripasudil, and netarsudil demonstrate efficacy in reducing macular thickness by inhibiting excessive leukocyte adhesion and vascular leakage, which contribute to retinal damage in DME. Rho kinase inhibitors emerge as a promising adjunct or alternative therapy for DME, particularly in non-responders to anti-VEGF treatments, though further clinical trials are required to establish optimal usage guidelines.[27] The limitations of the study include the heterogeneity of the extracted data, which shows varying responses to different combination therapies and trials should include a broader range of DME types, as this study focused only on naive DME.

CONCLUSION

Combination therapies (Laser or Diclofenac plus anti-VEGF) show superior efficacy in improving BCVA and reducing CMT in DME patients compared with anti-VEGF monotherapy, with manageable adverse events. Further trials assessing different combination therapy are needed to confirm our findings.

DISCLOSURES

Funding
None received.

Ethics Approval
Not Applicable.

Conflict of Interest
None to state.

Author Contribution
IBC was involved in conceptualization, methodology, validation, investigation, data curation, original draft preparation, supervision, and project administration. AFP was involved in software, formal analysis, resources, writing (review and editing), and visualization. All authors prepared and agreed to this final version of the manuscript for submission to this journal.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas. 9th ed. Brussels, Belgium; 2019.
2. Teo ZL, Tham YC, Yu M, Chee ML, Rim TH, Cheung N, et al. Global Prevalence of Diabetic Retinopathy and Projection of Burden through 2045: Systematic Review and Meta-analysis. Ophthalmology [Internet]. 2021 Nov 1 [cited 2025 Jun 9];128(11):1580–91. Available from: https://www.aaojournal.org/action/showFullText?pii=S0161642021003213

3. Tatsumi T. Current Treatments for Diabetic Macular Edema. Int J Mol Sci [Internet]. 2023 Jun 1 [cited 2025 Jun 9];24(11). Available from: https://pubmed.ncbi.nlm.nih.gov/37298544/
4. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ [Internet]. 2021 Mar 29 [cited 2025 Jun 1];372. Available from: https://www.bmj.com/content/372/bmj.n71
5. Ahmadieh H, Nourinia R, Hafezi-Moghadam A, Sabbaghi H, Nakao S, Zandi S, et al. Intravitreal injection of a Rho-kinase inhibitor (fasudil) combined with bevacizumab versus bevacizumab monotherapy for diabetic macular oedema: a pilot randomised clinical trial. British Journal of Ophthalmology [Internet]. 2019 Jul 1 [cited 2025 Jun 9];103(7):922–7. Available from: https://bjo.bmj.com/content/103/7/922
6. Fekri S, Rabiei A, Hooshmandi S, Nouri H, Abtahi SH. The effect of combination therapy with intravitreal bevacizumab and topical timolol-dorzolamide eye drops on diabetic macular edema: a double-blind randomized controlled trial. Int Ophthalmol [Internet]. 2024 Dec 1 [cited 2025 Jun 9];44(1). Available from: https://pubmed.ncbi.nlm.nih.gov/38376643/
7. Riazi-Esfahani M, Riazi-Esfahani H, Ahmadraji A, Karkhaneh R, Mahmoudi A, Roohipoor R, et al. Intravitreal bevacizumab alone or combined with 1 mg triamcinolone in diabetic macular edema: a randomized clinical trial. Int Ophthalmol [Internet]. 2018 Apr 1 [cited 2025 Jun 9];38(2):585–98. Available from: https://pubmed.ncbi.nlm.nih.gov/28349504/
8. Lim JW, Lee HK, Shin MC. Comparison of intravitreal bevacizumab alone or combined with triamcinolone versus triamcinolone in diabetic macular edema: A randomized clinical trial. Ophthalmologica [Internet]. 2012 Jan [cited 2025 Jun 9];227(2):100–6. Available from: https://www.researchgate.net/publication/51715189_Comparison_of_Intravitreal_Bevacizumab_Alone_or_Combined_with_Triamcinolone_versus_Triamcinolone_in_Diabetic_Macular_Edema_A_Randomized_Clinical_Trial
9. Neto HO, Regatieri C V., Nobrega MJ, Muccioli C, Casella AM, Andrade RE, et al. Multicenter, randomized clinical trial to assess the effectiveness of intravitreal injections of bevacizumab, triamcinolone, or their combination in the treatment of diabetic macular edema. Ophthalmic Surg Lasers Imaging Retina. 2017 Sep 1;48(9):734–40.
10. Adán A, Cabrera F, Figueroa MS, Cervera E, Ascaso FJ, Udaondo P, et al. Clinical-Decision Criteria to Identify Recurrent Diabetic Macular Edema Patients Suitable for Fluocinolone Acetonide Implant Therapy (ILUVIEN®) and Follow-Up Considerations/Recommendations. Clin Ophthalmol [Internet]. 2020 [cited 2025 Jun 1];14:2091. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7398681/
11. Downey L, Acharya N, Devonport H, Gale R, Habib M, Manjunath V, et al. Treatment choices for diabetic macular oedema: a guideline for when to consider an intravitreal corticosteroid, including adaptations for the COVID-19 era. BMJ Open Ophthalmol [Internet]. 2021 Apr 27 [cited 2025 Jun 1];6(1):e000696. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8088120/
12. Mehta H, Hennings C, Gillies MC, Nguyen V, Campain A, Fraser-Bell S. Anti-vascular endothelial growth factor combined with intravitreal steroids for diabetic macular oedema. Cochrane Database Syst Rev [Internet]. 2018 Apr 18 [cited 2025 Jun 9];2018(4):CD011599. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6494419/
13. Abdel-Maboud M, Menshawy E, Bahbah EI, Outani O, Menshawy A. Intravitreal bevacizumab versus intravitreal triamcinolone for diabetic macular edema–Systematic review, meta-analysis and meta-regression. PLoS One [Internet]. 2021 Jan 1 [cited 2025 Jun 9];16(1):e0245010. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7802957/
14. Whitcup SM, Cidlowski JA, Csaky KG, Ambati J. Pharmacology of Corticosteroids for Diabetic Macular Edema. Invest Ophthalmol Vis Sci [Internet]. 2018 Jan 1 [cited 2025 Jun 9];59(1):1. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5961100/
15. Grad J, Hatamnejad A, Dadak R, Sodhi S, Pattathil N, Choudhry N. Anti-VEGF Monotherapy vs Anti-VEGF and Steroid Combination Therapy for Diabetic Macular Edema: A Meta-analysis. J Vitreoretin Dis [Internet]. 2024 Jan 1 [cited 2025 Jun 9];24741264241280596. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11556321/
16. Zhou B, Liu H, Xiong F. Efficacy and safety of dexamethasone or triamcinolone in combination with anti-vascular endothelial growth factor therapy for diabetic macular edema: A systematic review and meta-analysis with trial sequential analysis. PLoS One [Internet]. 2025 Feb 1 [cited 2025 Jun 9];20(2). Available from: https://pubmed.ncbi.nlm.nih.gov/39919066/
17. Meng W, Li R, Xie X. Conbercept and Retinal Photocoagulation in the treatment of Diabetic Macular Edema. Pak J Med Sci [Internet]. 2019 Nov 1 [cited 2025 Jun 9];35(6):1493. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6861463/
18. Huang C, Ji H, Han X. The Effectiveness of Conbercept Combined with Panretinal Photocoagulation vs. Panretinal Photocoagulation in the Treatment of Diabetic Retinopathy: A Meta-Analysis. J Ophthalmol [Internet]. 2021 [cited 2025 Jun 9];2021:5591719. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8128542/
19. Bressler SB, Odia I, Glassman AR, Danis RP, Grover S, Robert Hampton G, et al. Changes in diabetic retinopathy severity when treating diabetic macular edema with ranibizumab DRCR.NET protocol I 5-year report. Retina [Internet]. 2018 [cited 2025 Jun 9];38(10):1896–904. Available from: https://journals.lww.com/retinajournal/fulltext/2018/10000/changes_in_diabetic_retinopathy_severity_when.2.aspx
20. Mitchell P, Bandello F, Schmidt-Erfurth U, Lang GE, Massin P, Schlingemann RO, et al. The RESTORE study: Ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. Ophthalmology [Internet]. 2011 Apr 1 [cited 2025 Jun 9];118(4):615–25. Available from: https://www.aaojournal.org/action/showFullText?pii=S0161642011000649
21. Nidya Sandra M, Shabrina Y, Wahyu Widayanti T, Ekantini R, Supartoto A, Bayu Sasongko M. CENTRAL MACULAR THICKNESS AFTER COMBINED THERAPY OF BEVACIZUMAB INTRAVITREAL INJECTION AND TOPICAL DICLOFENAC COMPARED WITH BEVACIZUMAB INTRAVITREAL INJECTION IN DIABETIC MACULAR EDEMA. International Journal of Retina (IJRETINA) 2021 [Internet]. 4(2). Available from: https://doi.org/10.35479/ijretina.2021.v
22. Ghanbari H, Kianersi F, Sonbolestan SA, Abtahi MA, Akbari M, Abtahi ZA, et al. Intravitreal Diclofenac plus Bevacizumab versus Bevacizumab alone in treatment-naive diabetic macular edema: a randomized double-blind clinical trial. Int Ophthalmol [Internet]. 2017 Aug 1 [cited 2025 Jun 9];37(4):867–74. Available from: https://link.springer.com/article/10.1007/s10792-016-0335-z
23. Supanji S, Ramania W, Sandra MN, Agni AN, Suhardjo S, Ekantini R, et al. Efek Penambahan Natrium Diklofenak Topikal pada Terapi Injeksi Intravitreal Bevacizumab terhadap Perubahan Visus dan Tekanan Intraokular Pasien dengan Edema Makula Diabetika. Ophthalmologica Indonesiana [Internet]. 2023 Aug 31 [cited 2025 Jun 9];49(2):122–31. Available from: https://www.ophthalmologica-indonesiana.com/index.php/journal/article/view/100270
24. Sridhar J, Hsu J, Shahlaee A, Garg SJ, Spirn MJ, Fineman MS, et al. Topical Dorzolamide-Timolol With Intravitreous Anti-Vascular Endothelial Growth Factor for Neovascular Age-Related Macular Degeneration. JAMA Ophthalmol [Internet]. 2016 Apr 1 [cited 2025 Jun 9];134(4):437–43. Available from: https://pubmed.ncbi.nlm.nih.gov/26914218/
25. Harris A, Ciulla TA, Pratt LM, Rechtman E, Kagemann L, Piper HC, et al. The effects of dorzolamide on choroidal and retinal perfusion in non-exudative age related macular degeneration. Br J Ophthalmol [Internet]. 2003 Jun 1 [cited 2025 Jun 9];87(6):753. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC1771708/
26. Mirshahi A, Tadayoni R, Mohsenzadeh N, Saeidi Rezvani T, Abrishami M. Efficacy of adjuvant topical timolol–dorzolamide with intravitreal bevacizumab injection in diabetic macular edema: A contralateral eye study. J Curr Ophthalmol [Internet]. 2019 Jun 1 [cited 2025 Jun 9];31(2):168. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6611985/
27. Mateos-Olivares M, García-Onrubia L, Valentín-Bravo FJ, González-Sarmiento R, Lopez-Galvez M, Pastor JC, et al. Rho-Kinase Inhibitors for the Treatment of Refractory Diabetic Macular Oedema. Cells [Internet]. 2021 Jul 1 [cited 2025 Jun 9];10(7). Available from: https://pubmed.ncbi.nlm.nih.gov/34359853/