

Recent Advances in The Management of Diabetic Macular Edema

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Abstract

Diabetic macular oedema (DME) is a vision-threatening complication of diabetic retinopathy caused by breakdown of the retinal vascular barrier and accumulation of intraretinal or subretinal fluid. Optical coherence tomography (OCT) has transformed diagnosis and treatment monitoring. Intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy remains the principal treatment for centre-involving DME, but repeated injections create a substantial burden for patients and health-care systems. Recent developments aim to improve durability without compromising vision. Faricimab, a bispecific antibody targeting VEGF-A and angiopoietin-2, permits personalised dosing intervals of up to 16 weeks in appropriately responding eyes. The ranibizumab port-delivery system (PDS) provides continuous drug delivery with refill exchanges every 24 weeks and was noninferior to monthly ranibizumab in the PAGODA randomised trial. Corticosteroid implants remain useful in selected eyes, particularly when anti-VEGF response is inadequate, although cataract formation and intraocular-pressure elevation require careful monitoring. This review summarises current evidence, practical treatment considerations, limitations, and future directions in sustained drug delivery for DME.

Keywords: Anti-VEGF, Corticosteroid implant, Diabetic macular oedema, Diabetic retinopathy, Optical coherence tomography, Port-delivery system, Ranibizumab.

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Introduction

Diabetic macular oedema is defined by retinal thickening or fluid involving the macula in the setting of diabetes. It may develop at any stage of diabetic retinopathy and remains an important cause of preventable central-vision loss. The underlying process includes hyperglycaemia-related endothelial dysfunction, inflammatory signalling, pericyte loss, and increased vascular permeability. These changes disrupt the inner blood-retinal barrier and allow fluid and lipid to accumulate within the neurosensory retina.^[1]

The reported prevalence varies according to the population studied, diabetes duration, glycaemic control, imaging method, and definition of oedema. A meta-analysis estimated that approximately 5.5% of people with diabetes have DME, while European primary-care data reported a prevalence of about 3.7%.^[1-3] Accordingly, broad claims of a single worldwide prevalence should be avoided unless the population and diagnostic method are specified.

Clinically, patients may be asymptomatic or report blurred or distorted central vision. Fundus examination can show microaneurysms, retinal thickening, hard exudates, and macular haemorrhage. OCT is central to contemporary care because it detects cystoid spaces, subretinal fluid, disorganisation of the retinal layers, and changes in central subfield thickness.^[4,5] Fluorescein angiography is helpful when the leakage pattern or an alternative diagnosis remains uncertain.

The Early Treatment Diabetic Retinopathy Study established the benefit of focal or grid laser for clinically significant macular oedema, particularly when oedema did not involve the foveal centre.^[6,7] For centre-involving DME with visual impairment, intravitreal anti-VEGF agents are generally used as first-line therapy. The choice among aflibercept, ranibizumab, and bevacizumab depends on visual acuity, availability, cost, safety, and local regulatory considerations.^[8-10]

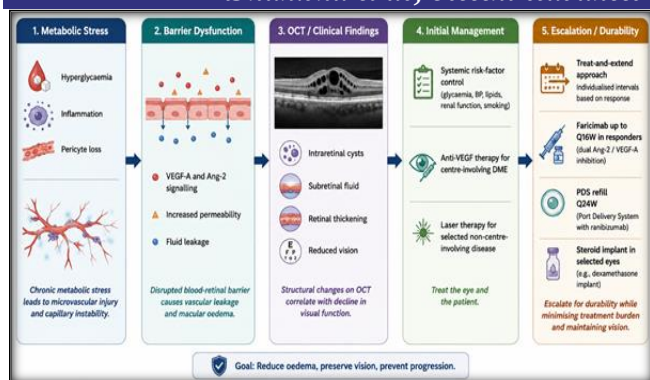


Figure 1: Pathophysiology and treatment pathway in diabetic Macular Edema (DME)

CURRENT TREATMENT STRATEGIES

Anti-VEGF therapy

VEGF is a major mediator of vascular leakage in diabetic retinopathy. Intravitreal aflibercept, bevacizumab, and ranibizumab improve visual acuity and reduce macular thickness, although the magnitude of benefit may differ according to baseline visual acuity. In Protocol T, aflibercept produced greater mean visual improvement at one year in eyes with worse baseline vision, whereas average differences were smaller among eyes with milder visual loss.^[8,9] Treatment usually begins with relatively frequent injections followed by a treat-and-extend, pro re nata, or disease-activity-guided regimen.

Laser photocoagulation

Laser remains relevant for selected non-centre-involving oedema and focal leaking microaneurysms. It is less effective than anti-VEGF therapy for centre-involving DME with visual loss and can cause retinal scarring or unwanted field defects if applied excessively.^[6,7]

Intravitreal corticosteroids

Corticosteroids reduce inflammatory mediators and vascular permeability. Triamcinolone, dexamethasone implants, and fluocinolone acetonide implants have been studied in DME. They are often considered when anti-VEGF response is insufficient, when injection frequency is impractical, or when an inflammatory component is suspected. The main limitations are cataract progression and raised intraocular pressure; therefore, lens status and glaucoma risk should influence treatment selection.^[11-15]

RECENT ADVANCES

Faricimab

Faricimab is a bispecific monoclonal antibody designed to simultaneously target vascular endothelial growth factor-A (VEGF-A) and angiopoietin-2 (Ang-2), thereby modulating two key pathways involved in retinal vascular dysfunction. In the YOSEMITE and RHINE phase 3 trials, faricimab administered every 8 weeks or according to a personalised treatment interval achieved visual outcomes that were noninferior to aflibercept, with dosing intervals extendable to as long as 16 weeks in suitable patients.^[16,17] The two-year data support durable visual and anatomical responses with personalised treat-and-extend treatment.^[18]

In clinical practice, faricimab should not be interpreted as an automatic four-monthly treatment for every patient. Interval

extension requires stable visual acuity and OCT findings, and some eyes continue to need shorter intervals. The U.S. prescribing information describes an initial monthly phase followed by disease-guided extension or an alternative fixed regimen; local labels may differ.^[19]

Ranibizumab port-delivery system

The ranibizumab PDS is an implanted reservoir designed to provide continuous intravitreal delivery, reducing the need for monthly injections. In the PAGODA randomised clinical trial, the PDS with 100 mg/mL ranibizumab and 24-week refill exchanges produced a mean best-corrected visual-acuity gain of 9.6 letters at weeks 60 and 64, compared with 9.4 letters for monthly ranibizumab, meeting the prespecified noninferiority criterion.^[20] However, device-related adverse events were more frequent than with injections, so implantation, refill procedures, monitoring, and patient selection are central to safe use.

Regimen	Delivery pattern	Potential advantage	Important considerations
Monthly anti-VEGF	Frequent intravitreal injections, adjusted to response	Established efficacy and flexible agent choice	Visit and injection burden; adherence and procedure-related risks
Faricimab treat-and-extend	Initial monthly treatment, then intervals extended by response, up to 16 weeks in trials	Dual VEGF-A/Ang-2 inhibitors; fewer visits for suitable responders	Not every eye reaches the longest interval; continued OCT monitoring
Ranibizumab PDS	Continuous delivery with refill exchanges every 24 weeks	Reduces injection frequency	Requires implantation and refill procedures; device-related adverse events

Figure: 2 Treatment burden comparison in Diabetic Macular Edema (DME)

Patient-Centered Treatment Planning

The best regimen is not determined by drug efficacy alone. (21-23) Treatment decisions should consider baseline visual acuity, OCT morphology, renal and cardiovascular comorbidity, pregnancy considerations, lens status, glaucoma risk, appointment access, affordability, and the patient's ability to attend follow-up. Systemic management of glycaemia, blood pressure, and lipids remains essential, because ocular treatment does not remove the underlying metabolic risk.

A practical pathway is to confirm centre involvement with OCT, address urgent coexisting pathology, begin an evidence-based intravitreal regimen when indicated, and reassess visual acuity and OCT response at each visit. If oedema persists, clinicians should confirm adherence, reconsider the diagnosis, evaluate tractional components, and discuss switching agents or adding a corticosteroid in an appropriate patient. Surgery is reserved for selected cases with vitreomacular traction, epiretinal membrane, or another surgically correctable cause.

Conclusion

CAG is generally the preferred grafting technique for primary pterygium because it is associated with lower recurrence and good cosmetic and functional outcomes. AMT remains an important option when conjunctiva must be

preserved or when a large ocular-surface defect requires biologic support. The final choice should account for disease severity, recurrence status, available conjunctiva, future glaucoma surgery, surgeon expertise, and patient-specific risk factors.

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