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Review

Management of Diabetic Retinopathy in Advanced Stages: A Brief Review

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ABSTRACT

Diabetic retinopathy (DR) is one of the leading causes of preventable blindness in adults worldwide. It is estimated that between 20% and 30% of patients with diabetes mellitus will develop some form of DR during their lifetime. In advanced stages characterized by proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) serious complications such as vitreous hemorrhage, tractional retinal detachment and aberrant neovascularization occur, significantly compromising visual acuity. Management of these conditions requires a multidisciplinary approach that includes strict metabolic control, intravitreal pharmacotherapy and surgical interventions. Anti-VEGF agentes such as ranibizumab, aflibercept and bevacizumab have demonstrated efficacy in reducing edema and stabilizing vision in the short- and medium-term, although their frequent administration and high cost may limit patient adherence. Intravitreal corticosteroids offer an alternative in cases of insufficient response to anti-VEGF therapy but carry risks of cataract and intraocular hypertension, necessitating careful monitoring. Panretinal photocoagulation remains the first-line method for controlling neovascularization in resource-limited settings, despite side effects like peripheral visual field constriction. Vitrectomy is indicated for persistent vitreous hemorrhage and tractional detachments, with better outcomes when combined with perioperative anti-VEGF treatment. Advances in diagnostics such as optical coherence tomography (OCT) and OCT angiography enhance disease monitoring and guide therapeutic decisions. However, socioeconomic and structural barriers, particularly in low- and middle-income countries, hinder access to these technologies and treatments, compromising prognosis. Finally, teleophthalmology and research into gene therapies and novel angiogenic modulators emerge as promising strategies to expand care coverage and improve long-term visual outcomes.

Keywords: Diabetic retinopathy; Vitrectomy; Macular edema; Anti-VEGF therapy; Ocular management

Introduction

Diabetes mellitus (DM) is a highly prevalent chronic condition affecting over 422 million people worldwide, posing a significant public health challenge[1]. Among the microvascular complications of DM, diabetic retinopathy (DR) stands out as one of the leading causes of irreversible visual loss in adults[2]. DR progresses through stages ranging from early microvascular

changes such as microaneurysms and retinal hemorrhages to advanced phases like proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME), both of which carry a high risk of blindness[3]. The pathophysiology of DR involves endothelial dysfunction, increased vascular permeability, retinal hypoxia and activation of angiogenic pathways, notably vascular endothelial growth factor (VEGF), which drives pathological neovascularization[2]. In early stages, strict glycemic control, antihypertensive therapy and correction of dyslipidemia effectively slow DR progression. However, once the disease reaches advanced stages, systemic management alone becomes insufficient. Local and invasive strategies become essential. Historically, panretinal photocoagulation (PRP) was the first intervention to arrest neovascularization in PDR, reducing the risk of vitreous hemorrhage but at the expense of peripheral visual field loss[4].

The advent of anti-VEGF agents ushered in a new era in DME and PDR treatment, characterized by macular thickness reduction, visual stabilization and partial regression of neovascularization albeit requiring frequent administration[5,6]. Intravitreal corticosteroid implants, such as dexamethasone, have emerged as alternatives in patients refractory to or contraindicated for anti-VEGF therapy, demonstrating efficacy but demanding vigilance for cataract formation and elevated intraocular pressure[7]. Surgically, vitrectomy has become essential for managing unresolved vitreous hemorrhages and tractional retinal detachments, with superior visual outcomes when combined with perioperative anti-VEGF injections[8,9].

Advances in diagnostics including optical coherence tomography (OCT) and OCT angiography allow precise measurement of retinal thickness, vascular mapping and early complication detection, guiding individualized treatment plans[10]. Nevertheless, implementation of these technologies and therapies faces barriers such as high cost, infrastructure requirements and specialist shortages, especially in middle- and low-income countries[11]. In this context, teleophthalmology shows promise by enabling large-scale screening and remote monitoring, potentially expanding early diagnosis and continuity of care in vulnerable populations. This review comprehensively examines current strategies for managing advanced DR, analyzing the benefits and limitations of each approach and highlighting future perspectives to optimize visual outcomes and reduce the socioeconomic burden of the disease.

Objectives

This article aims to review the most recent advances in the management of diabetic retinopathy in advanced stages, emphasizing the role of pharmacological therapies particularly anti-VEGF agents and intravitreal corticosteroids and the importance of surgical interventions such as vitrectomy in controlling vitreous hemorrhage and tractional retinal detachments.

Materials and Methods

A bibliographic review of articles published in PubMed, ScienceDirect and SciELO databases was conducted to support this study.

Discussion

The underlying pathophysiology of advanced DR involves chronic endothelial damage, increased vascular permeability and tissue hypoxia, leading to excessive production of VEGF and other proinflammatory cytokines[2]. This proangiogenic environment generates fragile new vessels prone to rupture, causing vitreous hemorrhages and tractional detachments, hallmarks of PDR[3]. DME arises from fluid extravasation into the macula due to a compromised blood–retinal barrier, resulting in progressive loss of central visual acuity[12]. Anti-VEGF therapies revolutionized DME treatment by selectively inhibiting VEGF activity, reducing macular edema and improving vision in multicenter trials[5,6]. However, the requirement for monthly injections poses adherence challenges, especially where travel to ophthalmic centers is difficult. Intravitreal corticosteroid implants such as dexamethasone and fluocinolone offer sustained drug release, reducing injection frequency but increasing cataract and intraocular pressure risks, necessitating periodic monitoring[7]. PRP remains relevant in low-resource settings due to its low cost and wide availability, despite adverse effects on peripheral vision[4].

Vitrectomy is well-established for persistent vitreous hemorrhage and tractional detachments and is enhanced by perioperative anti-VEGF use to minimize intraoperative bleeding and improve postoperative clarity[8,9]. Complementary diagnostic advances such as OCT angiography enable noninvasive visualization of retinal vascular plexuses, identifying ischemic areas and guiding focal treatments[10]. Nonetheless, unequal distribution of technological and human resources creates treatment disparities, worsening ocular morbidity in vulnerable populations (Silva et al., 2018). Teleophthalmology platforms have proven effective for screening and remote follow-up, reducing costs and expanding population coverage[11]. In translational research, gene therapies, non-VEGF pathway modulators and sustained-release drug delivery systems are emerging as future options for less invasive management with fewer interventions[13].

Conclusions

Advanced diabetic retinopathy presents clinical and social challenges due to complex vascular and tissue alterations that impair visual acuity. Anti-VEGF therapies have set a new paradigm in controlling DME and regressing neovascularization, yielding significant visual gains but requiring frequent injections that may compromise adherence[5,6]. Intravitreal corticosteroid implants provide prolonged drug delivery yet demand careful monitoring for cataract and intraocular hypertension[7]. Pan retinal photocoagulation remains valuable in low-resource contexts for its efficacy and low cost, despite peripheral field side effects[4]. Vitrectomy continues to be the procedure of choice for severe surgical complications, such as vitreous hemorrhage and tractional detachments, with optimized outcomes when combined with perioperative anti-VEGF agents[8,9].

Improved diagnostic techniques particularly OCT and OCT angiography allow more precise therapeutic planning, contributing to better visual outcomes[10]. However, socioeconomic and infrastructural barriers remain significant obstacles to accessing advanced treatments, especially in middle- and low-income countries[11]. Solutions such as teleophthalmology can broaden screening coverage and ensure continuous follow-up, reducing costs and easing the burden on specialized services. Future prospects include the development of gene therapies, novel angiogenic modulators and sustained-release devices, which promise to decrease intervention frequency and improve patient quality of life[13]. Additionally, public health policies focused on primary prevention and health education are essential to strengthen metabolic control and

reduce the incidence of advanced DR. In summary, combining pharmacological, surgical and technological advances with public health strategies and telemedicine is crucial to enhance the management of advanced diabetic retinopathy and mitigate its global impact on preventable blindness[14,15].

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