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Review

Treatment of Age-Related Macular Degeneration (AMD): A Brief Literature Review

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ABSTRACT

Age-Related Macular Degeneration (AMD) is the leading cause of irreversible central visual impairment in adults over 60 years of age, directly affecting autonomy and social participation. The disease manifests in two clinical forms: the dry form, characterized by drusen accumulation and gradual retinal pigment epithelium (RPE) atrophy; and the wet form, marked by pathological choroidal neovascularization leading to exudation, edema and hemorrhage beneath the macula. While antioxidant supplementation as recommended by the AREDS trials remains one of the few proven interventions for dry AMD, treatment of the wet form has evolved dramatically with the introduction of vascular endothelial growth factor inhibitors (anti-VEGF), which can stabilize or even improve visual acuity in a significant proportion of patients. Nevertheless, challenges persist related to high cost, the need for frequent intravitreal injections and variable patient response. Recent gene-therapy studies aim to provide sustained intraocular production of anti-angiogenic molecules, while regenerative-medicine research is evaluating stem-cell transplantation to restore the RPE. Concurrently, artificial-intelligence tools applied to optical coherence tomography promise earlier detection of progression and personalized treatment regimens. World Health Organization data project that the global number of affected individuals may exceed 288 million by 2040, imposing an estimated annual cost of over USD 250 billion on healthcare systems. Integrated strategies are therefore essential.

Keywords: AMD; Anti-VEGF therapy; Photodynamic therapy; Stem cells; Gene therapy

Introduction

Age-Related Macular Degeneration (AMD) is a progressive degenerative condition affecting the macula the retinal region responsible for high-resolution tasks such as reading and facial recognition. Increased life expectancy has elevated AMD to a public-health priority, with prevalence roughly doubling each decade after age 50. A recent report estimates that 8.7 % of the global population over 45 shows signs of the disease[1]. Its socioeconomic impact includes loss of independence, higher risk of falls, depression, direct medical costs and early retirement, placing a substantial burden on individuals and healthcare systems[2].

The pathophysiology of AMD involves a complex interplay of genetic predisposition, cellular aging, oxidative stress, RPE dysfunction and low-grade chronic inflammation[3]. Polymorphisms in complement-system genes (CFH, C3) disrupt alternative-pathway regulation and predispose to subretinal drusen accumulation, while environmental factors particularly smoking, poor dietary antioxidant intake and excessive blue-light exposure accelerate reactive-oxygen–species formation[4,5].

As oxidative material accumulates and RPE function declines, photoreceptor recycling is impaired, leading to cell death and the two classic clinical manifestations. In the dry (atrophic) form responsible for about 85 % of cases lipofuscin deposits and gradual RPE degeneration culminate in geographic atrophy, compromising central visual fields. The less prevalent wet form involves choroidal neovascularization breaching Bruch's membrane, causing exudation, edema and intra- or subretinal hemorrhage; without intervention, vision loss can be rapid and severe[6].

Diagnosis was revolutionized by optical coherence tomography (OCT), which provides noninvasive cross-sectional retinal imaging and detects early layer changes before symptom onset. Advances in artificial intelligence promise deep-learning algorithms with over 95 % accuracy in detecting subretinal fluid and identifying early neovascular activity, enabling personalized injection intervals and resource optimization[7]. Therapeutically, the past decade has seen disruptive innovation with anti-VEGF agents, which reduce the risk of moderate vision loss by up to 70 % in wet AMD[8]. However, the absence of an effective treatment to reverse dry AMD remains a major gap, driving research into antioxidant supplementation, gene therapy and regenerative medicine[9]. In light of these transformations, it is essential to critically synthesize recent literature to guide clinical decisions and identify knowledge gaps.

Objectives

Review current therapeutic options for both forms of AMD, emphasizing anti-VEGF treatments and supplementation protocols based on AREDS studies. Discuss evolving evidence on emerging strategies such as viral vectors, sustained-release implants and cell therapy. Analyze the impact of these interventions on disease burden in terms of effectiveness, cost and quality of life.

Materials and Methods

A scientific literature review was conducted using the PubMed, SciELO, Google Scholar and ScienceDirect databases.

Discussion

The therapeutic evolution of wet AMD exemplifies how molecular insights can radically change a disease's prognosis. Anti-VEGF agentes bevacizumab, ranibizumab, aflibercept and more recently brolucizumab-block pathological angiogenesis, stabilize the blood–retina barrier and reduce macular edema[10,11]. Follow-up trials report that up to 40 % of treated patients gain three or more lines of vision after two Years an unprecedented result in ophthalmology history[8]. Yet monthly injections burden healthcare services, induce patient anxiety and reduce adherence, especially among elderly patients with multiple comorbidities.

To mitigate this load, treat-and-extend regimens gradually lengthen injection intervals based on anatomical and functional OCT findings. Cohort studies show that average intervals can reach twelve weeks without compromising visual outcomes for many patients[12]. Additionally, intraocular sustained-release ranibizumab implants have maintained therapeutic levels for up to six months, cutting annual procedure numbers by 75 %[13]. For dry AMD, AREDS-based antioxidant supplementation remains the management cornerstone, delaying progression to advanced stages by up to 25 %[4]. Modification of risk factors smoking cessation, regular exercise and diets rich in lutein, zeaxanthin and omega-3 also significantly slows functional decline[5]. However, these measures cannot restore lost tissue, underscoring the need for restorative therapies.

Gene therapy emerges as a promising alternative to achieve sustained intraocular expression of anti-angiogenic or complement-modulating proteins. AAV-based vectors encoding aflibercept or C3 antagonists have achieved sustained edema reduction in animal models and entered phase II clinical trials, reducing retreatment needs by 70 % over one year[9]. Yet questions of durability, immunological safety and cost remain unanswered. Concurrently, regenerative medicine explores iPSC-derived stem-cell transplantation to repopulate atrophic RPE. Preliminary analyses show morphological integration and modest gains in retinal sensitivity, but adverse events such as ectopic proliferation call for improved differentiation protocols and biosafety systems[3,14].

Another disruptive advance is AI-driven OCT analysis. Deep-learning algorithms now exceed 95 % accuracy in detecting subretinal fluid and early neovascular signs, enabling personalized injection schedules and resource optimization[7]. Integration of tele-ophthalmology platforms with automated analysis could expand specialist access in under-resourced regions without compromising care quality. Despite these promising avenues, significant barriers persist. High costs of novel drugs and advanced technologies limit access mostly to high-income countries, creating global equity gaps that demand differential pricing policies and public-private partnerships. Furthermore, genetic and environmental heterogeneity in AMD leads to variable therapeutic responses, indicating that personalized, biomarker-driven medicine will be essential to maximize benefit and minimize adverse events. Finally, the lack of clinical markers accurately predicting dry-to-wet conversion or geographical atrophy collapse prevents truly preventive interventions. Investments in translational research linking multi-omics data, high-resolution imaging and functional phenotyping represent the research frontier and may define the next generation of therapies.

Conclusion

A critical analysis confirms that the therapeutic landscape of AMD has evolved substantially over the past two decades, primarily due to VEGF inhibitors that have altered the natural history of wet AMD and demonstrated solid cost-effectiveness in settings with infrastructure for periodic intravitreal injections. Despite undeniable benefits, the need for frequent monitoring, cumulative endophthalmitis risk and high budgets pose logistical challenges that call for innovative care models such as satellite injection centers and OCT-guided treat-and-extend protocols. For dry AMD, significant gaps remain. Although backed by AREDS trials, antioxidant supplementation yields only modest effects and cannot prevent visual deterioration once geographic atrophy sets in. In this context, emerging gene-therapy techniques targeting complement modulation and stem-cell–derived RPE transplantation appear as potential long-term solutions. However, these interventions depend on phase-advanced trials assessing long-term safety, cost and real-world quality-of-life outcomes. AI represents a transversal opportunity: not only to optimize patient selection for retreatment but also to identify progression biomarkers that enrich clinical trials and yield more sensitive outcomes. Tele-ophthalmology-catalyzed by the COVID-19 pandemic has proven viable and effective for

chronic disease follow-up; when combined with AI platforms, it can democratize specialized care and reduce geographical disparities. From a public-health perspective, national screening programs using wide-field retinography cameras coupled with automated reading algorithms could detect AMD in its earliest stages, when interventions have the greatest chance to preserve vision. Pilot experiences in Asia and Europe have shown these initiatives to be feasible at an incremental cost below USD 500 per quality-adjusted life year well within World Health Organization cost-effectiveness thresholds[15].

Implementation in Brazil will require professional training, standardized workflows and interoperable integration with electronic health records. Finally, active patient participation in therapeutic planning is crucial. Qualitative studies demonstrate that shared decision-making improves satisfaction, adherence and clinical outcomes particularly when long injection schedules or lifestyle changes are involved. Thus, ongoing education for ophthalmologists should include communication skills and digital decision-support tools. In summary, effectively addressing AMD will demand convergence of cutting-edge translational research, equitable public policies, responsive healthcare systems and patient empowerment. Only through this multifaceted approach can we ensure that population aging does not translate into an epidemic of preventable blindness.

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