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DIABETIC RETINOPATHY AND MODERN THERAPEUTIC APPROACHES: STRATEGIES FOR PREVENTING AND CONTROLLING DISEASE PROGRESSION

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Abstract: Diabetic retinopathy (DR) is one of the main chronic complications of diabetes mellitus and is among the leading causes of visual loss and avoidable blindness in adults of working age worldwide. The aim of this study is to develop a study of diabetic retinopathy and modern therapeutic approaches, identifying the main strategies for preventing and controlling the progression of the disease. The methodological approach adopted in the study was a literature review, using databases of scientific articles that contributed to the theoretical basis of the work. The results indicate that progress in ocular therapy has brought new possibilities with the use of anti-VEGF agents, intravitreal corticosteroids and, more recently, with the introduction of gene therapies and nanotechnology-based treatments, which have broadened the prospects for safer, longer-lasting interventions with fewer side effects. The conclusion is that tackling diabetic retinopathy requires a comprehensive approach involving prevention, early diagnosis, therapeutic innovation and public health policies aimed at the comprehensive care of people with diabetes. By joining forces between health professionals, researchers and public managers, it is possible to considerably reduce the visual and socio-economic burden imposed by this serious complication of diabetes.
Keywords: Diabetic retinopathy. Diabetes mellitus. Blindness.

INTRODUCTION

Diabetic retinopathy (DR) is one of the main chronic complications of diabetes mellitus and is among the leading causes of visual loss and avoidable blindness in adults of working age worldwide. The disease is characterized by progressive changes in the retinal blood vessels caused by prolonged exposure to hyperglycemia. Initially asymptomatic, DR progresses silently, gradually compromising the patient's visual acuity as the retinal microvasculature suffers irreversible damage (Moraes *et al*., 2024).

The pathophysiology of DR involves multiple interconnected mechanisms, in which chronic hyperglycemia leads to endothelial dysfunction, increased vascular permeability, the formation of microaneurysms and areas of non-perfusion, as well as the release of pro-inflammatory cytokines and vascular endothelial growth factor (VEGF), responsible for abnormal neovascularization. As the disease progresses, complications arise such as vitreous hemorrhages, retinal detachment and neovascular glaucoma, which can result in permanent blindness (Tanuri *et al.,* 2023).

In the therapeutic context, traditional treatment methods, such as laser photocoagulation, still play an important role, especially in cases of proliferative diabetic retinopathy. However, the advent of intravitreal pharmacological therapies represented a milestone in modern ophthalmology (Cabellino *et al*., 2024).

Anti-VEGF agents such as ranibizumab, aflibercept and bevacizumab have been shown to be effective in reducing diabetic macular edema and regressing anomalous vessels, providing significant improvements in visual acuity and quality of life. In addition, intravitreal corticosteroids such as the dexamethasone implant are also used, especially in patients refractory to anti-VEGF or with contraindications to these drugs (Carvalho et al., 20230.

More recently, research such as that by Cabellino *et al*. (2024) has been exploring gene therapies, stem cell therapy, nanoparticles and new drug delivery routes that can offer longer duration of action with less frequent applications, as well as fewer adverse effects. These promising approaches are still in the study and development phase, but they point to a more personalized and efficient therapeutic future.

However, the effectiveness of any treatment depends above all on early diagnosis, so preventive strategies based on intensive glycemic

control, maintenance of blood pressure and lipid levels, smoking cessation and regular physical activity have had a direct impact on preventing DR and reducing the progression of the most severe forms of the disease. Adherence to treatment and periodic ophthalmologic follow-up are also decisive factors (Corsini *et al*., 2023).

In addition, the incorporation of digital technologies, such as telemedicine and artificial intelligence applied to screening and diagnostic imaging, has increased access to early screening for retinopathy, especially in remote regions or those with a shortage of specialists. This allows for early intervention and better allocation of health resources (Tochetto *et al*., 2024).

Therefore, the aim of this work is to develop a study on diabetic retinopathy and modern therapeutic approaches, identifying the main strategies for preventing and controlling the progression of the disease.

MATERIAL AND METHODS

The aim of this study was to gather, analyze and synthesize the available scientific knowledge on diabetic retinopathy, its modern therapeutic approaches and strategies aimed at preventing and controlling the progression of the disease. The review sought to identify recent advances in the field, as well as highlighting the most effective clinical approaches described in the specialized literature.

Data was collected from electronic scientific databases such as PubMed, SciELO (Scientific Electronic Library Online) and LILACS (Latin American and Caribbean Health Sciences Literature). The health science descriptors (Decs) used in the search were: "diabetic retinopathy", "therapeutic approaches", "modern treatments", "anti-VEGF", "prevention of diabetic retinopathy", "control of disease progression", "innovative therapies" and their English counterparts, using Boolean operators (AND, OR) to refine the results.

The review included articles published between 2019 and 2024, written in Portuguese, English or Spanish, which directly and objectively addressed the proposed topic. Priority was given to selecting original articles, systematic reviews, meta-analyses and up-to-date clinical guidelines with recognized relevance in the field of ophthalmology.

Duplicate papers, studies with inadequate methodology, abstracts from scientific events, theses and dissertations that did not present consistent data or were outside the thematic scope of the research were excluded.

After screening the titles and abstracts, the selected articles were read in full and their data was organized into thematic categories to allow a critical and comparative analysis of the information. The evidence was systematized in a descriptive way, based on the main findings on forms of prevention, drug therapies, surgical techniques and technological innovations in the treatment of DR, as well as the challenges faced in current clinical practice.

This study did not involve direct experimentation on humans or animals, but was merely a documentary analysis of previously published studies. For this reason, it was not necessary to submit it to the Research Ethics Committee.

RESULTS AND DISCUSSION

The analysis of the studies reviewed shows different therapeutic approaches and strategies for the prevention and control of diabetic retinopathy. Maturi *et al.* (2023) conducted a clinical trial with 328 adults with moderate to severe diabetic retinopathy, comparing the effects of treatment with intravitreal aflibercept versus placebo over four years.

The main metric evaluated was visual acuity, the results of which indicated a mean change of -2.7 (6.5) letters in the aflibercept group and -2.4 (5.8) letters in the placebo group. The rates of cardiovascular and cerebrovascular

events, according to the *Antiplatelet Trialists' Collaboration* criteria, were 9.9% for participants with bilateral involvement, 10.9% for those who received unilateral aflibercept and 7.8% for those treated with unilateral placebo (Maturi *et al*., 2023).

Although aflibercept promoted significant anatomical improvements in patients without central diabetic macular edema, these changes did not translate into significant visual benefits after four years of follow-up (Maturi et al., 2023).

In another study, IPP *et al*. (2021) evaluated the accuracy and safety of the automated EyeArt system (version 2.1.0), based on artificial intelligence, for detecting diabetic retinopathy more than mild (mtmDR) and at risk of visual loss (vtDR). A total of 942 adult subjects took part in the study. Initial imageability without dilation was 87.4%, rising to 97.4% after dilation according to the protocol developed.

After adjusting for sample enrichment, specificity for mtmDR reached 87.8%, while sensitivity remained high. For cases at risk of visual loss, both sensitivity and specificity were improved (IPP *et al.,* 2021).

The authors also point out that the technology has demonstrated high diagnostic performance without the need for medical mediation, offering a promising resource for expanding access to ophthalmic screening for diabetic patients and significantly speeding up the referral of critical cases (IPP *et al.,* 2021).

Motz *et al.* (2020) proposed an innovative approach for the early detection of diabetic retinopathy by analyzing oscillatory potential delays using a portable electroretinograph (RETeval). The sample consisted of individuals with diabetes without clinical signs of retinopathy, compared to controls of the same age group.

Significant delays in the implicit time of oscillatory potentials were observed in diabetic patients. After two weeks of treatment with levodopa (Sinemet), the electrophysiological parameters normalized, and the effects were maintained even after a washout period (Motz *et al*., 2020).

The authors suggest that such functional delays may serve as early biomarkers of retinal dysfunction and that treatment such as levodopa may have a reversible neuroprotective effect on the patient's retina (Motz *et al*., 2020).

Additionally, Goldberg *et al.* (2022) investigated the factors associated with the progression of diabetic retinopathy with less frequent use of ranibizumab after an induction phase with monthly injections.

The study concluded that patients who had more advanced forms of diabetic retinopathy at the start of treatment and who reached mild to moderate non-proliferative retinopathy (NPRD) had a higher risk of subsequent worsening compared to those who were already in less severe stages at the start of the study and were allocated to the placebo group (Goldberg *et al*., 2022).

According to Goldberg *et al.* (2022), the majority of patients treated with ranibizumab on a pro re nata (PRN) basis - i.e. according to clinical need - showed maintenance or improvement in their Diabetic Retinopathy Severity Scale (DRSS) scores, even with an injection frequency of less than monthly. The authors point out, however, that some form of continuous monitoring or minimal treatment may be necessary to preserve the benefits obtained after the initial induction phase.

In the study conducted by Preiss *et al*. (2024), the impact of fenofibrate on the progression of diabetic retinopathy was evaluated. The study, which involved 1,151 randomized participants, compared the group treated with fenofibrate to the placebo group. The rates of progression of retinopathy or maculopathy were 32.1% in the treated group and 40.2% in the control group, while the development of macular edema was observed in 3.8% and 7.5% of participants, respectively.

The results indicated that fenofibrate has a protective effect on the progression of diabetic retinopathy, particularly in individuals with early retinal manifestations (Preiss *et al*., 2024).

Rijal *et al.* (2022) conducted a study in which they investigated the effects of phacoemulsification in patients with previously untreated non-proliferative diabetic retinopathy, without the concomitant use of anti-vascular endothelial growth factor (anti-VEGF) agents.

The study sample included 32 eyes of 20 patients, with a mean age of 69.2 years, who underwent cataract surgery without complications. The authors observed that the surgery did not cause an increase in central macular thickness in the postoperative period, suggesting that the administration of anti-VEGF as an adjuvant measure in such cases is not mandatory (Rijal *et al*., 2022).

Zhou *et al.* (2021) evaluated the efficacy and safety of the combination of Qiming granules and laser photocoagulation in the management of diabetic retinopathy, with a 12-month clinical follow-up after six months of intervention. The authors report that the Qiming granule, a herbal medicine widely used in traditional Chinese medicine, works by benefiting Qi, nourishing organs such as the liver and kidneys, clearing collaterals and promoting eye health.

It also has immunomodulatory effects, stimulates cell growth, improves microcirculation and contributes to lowering blood glucose and lipid levels. For these reasons, it has become one of the most widely used patented herbal therapies in China for the treatment of diabetic retinopathy (Zhou *et al*., 2021).

Afarid *et al*. (2022) carried out a clinical study with the aim of evaluating the efficacy of garlic tablets (Allium sativum L.) as a complementary herbal therapy in the treatment of diabetic retinopathy. The study involved 91 participants, who were randomized to receive garlic tablets (500 mg, administered twice a day) or placebo over a period of four weeks.

At the end of the intervention, the patients were evaluated by specialized ophthalmologists. The main clinical outcomes measured included corrected visual acuity (CVVA, measured in logMAR), central macular thickness (CME, in micrometers) and intraocular pressure (IOP) (Afarid *et al*., 2022).

The results showed that garlic supplementation improved visual acuity, reduced central macular thickness and lowered intraocular pressure, suggesting its potential as an adjuvant treatment for diabetic retinopathy. In addition, the use of the herbal compound showed a satisfactory safety profile, with no relevant clinical adverse effects that would justify discontinuing treatment (Afarid *et al.,* 2022).

Tackling diabetic retinopathy therefore requires a comprehensive approach involving prevention, early diagnosis, therapeutic innovation and public health policies aimed at the comprehensive care of people with diabetes. By joining forces between health professionals, researchers and public managers, it is possible to considerably reduce the visual and socio-economic burden imposed by this serious complication of diabetes.

CONCLUSION

Throughout this work, we have seen that diabetic retinopathy is one of the main microvascular complications of diabetes mellitus and is one of the main causes of avoidable blindness in the world. The understanding of the pathophysiology of DR has evolved significantly in recent decades, revealing the complex interaction between chronic hyperglycemia, oxidative stress, inflammation and vascular dysfunction. These advances have enabled the development of increasingly specific and effective therapeutic approaches.

In the context of preventing and controlling the progression of DR, the importance of ri-

gorous management of systemic risk factors, such as glycemic, blood pressure and lipid control, coupled with adherence to treatment and regular ophthalmic monitoring, is highlighted.

At the same time, progress in ocular therapy has brought new possibilities with the use of anti-VEGF agents, intravitreal corticosteroids and, more recently, the introduction of gene therapies and nanotechnology-based treatments, which have broadened the prospects for safer, longer-lasting interventions with fewer side effects.

Although modern treatments have proven effective in stabilizing and regressing retinal lesions, early diagnosis remains the fundamental pillar in the fight against blindness caused by DR. The incorporation of technologies such as artificial intelligence and telemedicine in population screening is showing promise, especially in regions with limited access to specialized services.

In view of the above, it can be concluded that tackling diabetic retinopathy requires a multidisciplinary approach, combining prevention, health education, continuous surveillance and therapeutic innovation. Only by integrating science, technology and public health policies will it be possible to significantly reduce the impact of this disease on the quality of life of diabetic patients.

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