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Management of retinal diseases, therapeutic association between ophthalmology and endocrinology in the treatment of diabetic retinopathy

Manejo de doenças da retina, associação terapêutica entre oftalmologia e endocrinologia no tratamento da retinopatia diabética

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ABSTRACT

Introduction: Effective management of retinal diseases, especially diabetic retinopathy, is crucial to prevent severe visual complications. Collaboration between ophthalmologists and endocrinologists plays a key role in the effective treatment of this condition, aiming to preserve vision and improve the quality of life of patients. Methods: A literature review was conducted to understand the management of retinal diseases and the therapeutic association between ophthalmology and endocrinology in the treatment of diabetic retinopathy. We use databases such as MEDLINE, PubMed and Scielo to identify relevant articles published in the last 20 years. Inclusion and exclusion criteria were defined to ensure the selection of relevant studies.

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Results: After searching and selecting the articles, we identified patterns and trends in the management of diabetic retinopathy. A variety of treatment options have been located, including laser photocoagulation, intravitreal drug injections, and vitreoretinal surgery. The importance of metabolic control of diabetes to prevent damage to the retina is noted. The analysis of the studies also highlighted that the interaction between these specialties ensures better clinical outcomes. Conclusion: The importance of collaboration between ophthalmologists and endocrinologists in the management of diabetic retinopathy is reinforced. An integrated approach that considers both the ophthalmological and endocrinological aspects of the disease is essential to provide effective patient care. This cooperation can result in improved visual outcomes and quality of life for those affected by diabetic retinopathy.

Keywords: Diabetes mellitus, Clinical association, Diabetic retinopathy.

INTRODUCTION

The retina, crucial for vision, is susceptible to a variety of diseases, with diabetic retinopathy being one of the most prevalent and worrisome, especially in patients with diabetes mellitus (Schellini et al., 2014). Effective management of this condition requires an approach that integrates the knowledge of ophthalmology and endocrinology. The interaction between these two specialties is critical for the proper treatment of diabetic retinopathy, since strict glycemic control, along with preventive measures and ophthalmic therapeutics, can slow the progression of the disease and reduce the risk of severe visual complications.

Several studies have been conducted in order to investigate different treatment modalities, from pharmacological interventions to surgical approaches, aiming to preserve retinal health and maintain patients' quality of life (Mohamed et al., 2007). The therapeutic association between ophthalmology and endocrinology becomes evident in the use of pharmacological agents such as fenofibrate and semaglutide, which have demonstrated significant benefits in reducing the risk and progression of diabetic retinopathy (Kataoka et al., 2023; Wang et al., 2021).

Patient adherence to treatment and understanding of risk factors are crucial aspects, highlighting the importance of multidisciplinary education and support to achieve better clinical outcomes (Jannuzzi et al., 2014). This work aims to address the relevance of collaboration between ophthalmologists and endocrinologists in the integrated management of diabetic retinopathy, emphasizing the need for a holistic and personalized approach for each patient.

MATERIALS AND METHODS

A literature review was conducted with the objective of understanding the management of retinal diseases and the therapeutic association between ophthalmology and endocrinology in the treatment of diabetic retinopathy. Articles published in scientific journals were reviewed to provide a comprehensive view of the topic.

The data search was performed in the MEDLINE database, using the PubMed and Scielo search platforms. Search terms included combinations of keywords related to diabetic retinopathy, management, ophthalmology, and endocrinology. The search was restricted to studies published in the last 20 years to ensure the relevance of the data, and was conducted with the following inclusion and exclusion criteria:

INCLUSION CRITERIA

- Studies addressing the management of retinal diseases.
- Articles describing the treatments available for diabetic retinopathy.
- Studies that analyze the treatment options available for diabetic retinopathy in terms of ophthalmology and endocrinology.
- Research published in peer-reviewed scientific journals.
- Studies available in English, Spanish and Portuguese.

EXCLUSION CRITERIA

- Studies that do not focus on the pathologies of the reina, specifically diabetic retinopathy.
- Isolated case reports that do not provide relevant information on management for diabetic retinopathy.
- Duplicate or repeated studies.
- Articles not available in full or without free access.

The search strategy was developed using a combination of search terms related to the management of retinal diseases, and the therapeutic association between ophthalmology and endocrinology in the treatment of diabetic retinopathy. Boolean operators were used to optimize search accuracy and ensure that all relevant articles are identified. The descriptors used were: "Retinal Diseases"; "Diabetic Retinopathy"; "Treatment" and 2,153 articles were found. After adding the filter: "since 2005", 1,679 articles were found. After selecting based on relevant titles, methodology, objectives and results, a compilation of 97 articles was obtained to be analyzed.

The identified studies were initially reviewed based on their titles and abstracts to determine their relevance to the topic in question. The selected articles were then analyzed in full to confirm their inclusion in the literature review. Relevant data were extracted from the selected articles, including information on the management of retinal diseases, and the therapeutic association between ophthalmology and endocrinology in the treatment of diabetic retinopathy. The extracted data were analyzed qualitatively and synthesized in a narrative way.

Patterns and trends in the management of retinal diseases were identified, specifically diabetic retinopathy, and the results were presented in an organized and understandable manner. The methodological quality of the included studies was assessed using specific criteria for each type of study. Aspects such as the study design, the representativeness of the sample, and the analysis methodology were considered.

This literature review is based on the analysis of previously published data and does not involve the collection of information directly from human participants. Therefore, no additional ethical considerations are required. The results of this literature review will be presented in a scientific manuscript for publication in a peer-reviewed journal. The findings may also be shared at relevant scientific conferences and disseminated to health professionals interested in the topic.

RESULTS AND DISCUSSION

The following table presents a summary of the main studies related to the management of diabetic retinopathy, highlighting the therapeutic approaches, clinical outcomes, and relevant conclusions of these studies. These studies address a variety of interventions, from pharmacological treatments to epidemiological analyses, providing a comprehensive overview of the strategies used to prevent, control, and treat this ocular complication associated with diabetes mellitus. The analysis of these results contributes significantly to the understanding of the efficacy and safety of available therapies, as well as to the identification of gaps in knowledge and areas for future research.

Table 1: Relevant results

TITLE	AUTHOR, YEAR	OBJECTIVES	RESULTS	CONCLUSIONS
Management of diabetic retinopathy: a systematic review	MOHAMED; GILLIES; WONG, 2007	Review the best evidence for primary and secondary intervention in the treatment of DR, including diabetic macular edema.	Panretinal laser photocoagulation reduces the risk of moderate and severe visual loss by 50% in patients with severe proliferative and nonproliferative retinopathy. Laser focal photocoagulation reduces the risk of moderate visual loss by 50% to 70% in eyes with macular edema. Early vitrectomy improves visual recovery in patients with proliferative retinopathy and severe vitreous hemorrhage.	Strict control of blood glucose and blood pressure remains the cornerstone in the primary prevention of DR. Panretinal and focal laser photocoagulation of the retina reduce the risk of visual loss in patients with severe DR and macular edema, respectively. There is currently insufficient evidence to recommend the routine use of other treatments.
Fenofibrate for diabetic retinopathy	KATAOKA; LOIS; KAWANO; KATAOKA; INOUE; WATANABE , 2023	To investigate the benefits and harms of fenofibrate in preventing the development and progression of diabetic retinopathy in people with type 1 (T1D) or type 2 (T2D) diabetes, compared to placebo or observation	The use of fenofibrate increased serious adverse effects (RR 1.55; 95% CI 1.05 to 2.27; 2 studies, 15,313 participants; high-quality evidence). The studies did not report the incidence of a reduction in visual acuity of 10 letter ETDRS or more, the incidence of proliferative diabetic retinopathy, or the median vision-related quality of life.	Current moderate-quality evidence suggests that in a mixed group of people with and without overt retinopathy, who are living with T2D, fenofibrate is likely to result in little or no difference in the progression of diabetic retinopathy. However, in people with overt retinopathy living with T2D, fenofibrate is likely to slow progression. Serious adverse events were rare, but the risk of their occurrence was increased by the use of fenofibrate.
Treatment of diabetic retinopathy: perceptions of patients in Rio Claro (SP) - Brazil	SILVA; TEMPORINI; MOREIRA FILHO; KARA-JOSÉ, 2005	To identify the knowledge and opinions of a group of diabetic patients regarding diabetic retinopathy and its treatment in order to provide information that can contribute to the implementation and/or improvement of programs and preventive and control actions for this eye disease.	The sample consisted of 299 subjects aged between 16 and 83 years, with a mean age of 57 years, with a predominance of females (67.91%). They were unaware of the severity of their condition (30.8%), or considered it not serious (19.7%); Laser treatment of diabetic retinopathy was known by 60.2%, being cited as the only treatment by 24.1%. Among the reasons for the lack of treatment, the absence of feeling the need (59.8%) and the lack of financial resources (29.7%) stood out.	The subjects manifested a marked lack of knowledge about diabetic retinopathy, laser treatment and severity of the condition; Regardless of believing in the efficacy of the treatment, they were afraid to undergo it.

Risk of semaglutide and diabetic retinopathy in patients with type 2 diabetes mellitus: a meta-analysis of randomized controlled trials	WANG; MAO; WANG; LIU; HUANG, 2021	This study aimed to evaluate the association between semaglutide and the risk of retinopathy in patients with T2DM.	We included 23 randomized trials involving 22,096 patients with T2DM. There were 730 incident cases of DR – 463 in the semaglutide group and 267 in the control group. Overall, semaglutide was not associated with increased risk of DR compared to controls when all trials were combined (RR 1.14, 95% CI 0.98-1.33).	Semaglutide was not associated with an increased risk of DR; however, caution is required regarding the risk of DR for elderly patients or those with long-standing diabetes when taking semaglutide.
Is there any relationship between the results of the first day of anti-VEGF therapy for macular edema due to vascular disease and the long-term outcome?	GUNAY; ERDOGAN; AKALIN; KALKISIM; ESENULKU; 2024 UPDATED 2024 (GUNAY)	To evaluate the early changes after the first injection of anti-vascular endothelial growth factor (anti-VEGF) antibodies in cases of macular edema secondary to diabetic retinopathy and retinal vein occlusion and the relationship between these changes and the long-term outcome.	A total of 26 (44.8%) patients with macular edema and retinal vein occlusion and 32 (55.2%) patients with macular edema and diabetic retinopathy were registered. The mean follow-up time was 24.0 months (standard deviation of 8.5 months). A statistically significant decrease in central macular thickness was observed after anti-vascular endothelial growth factor treatment in both patients with macular edema and retinal vein occlusion and those with macular edema and diabetic retinopathy ($p<0.001$ for both). All patients with macular edema and retinal vein occlusion responded well on the 1st day post-injection	The long-term anatomical outcome of macular edema secondary to retinal vein occlusion and diabetic retinopathy can be predicted by response to treatment on day 1 after injection of vascular endothelial growth factor anti-vascular.
Medication adherence and quality of life in older adults with diabetic retinopathy	JANNUZZI; CINTRA; RODRIGUES; SAINT JOHN; GALLANI, 2014	To investigate the factors related to medication adherence and its relationship with health-related quality of life in older adults with diabetic retinopathy	The majority (58%) reported the use of 80% or more of the prescribed doses and the care taken when taking the medications. The item "discontinuing the use of medications because feeling worse" of the Morisky Scale explained 12.8 and 13.5% of the variability in the proportion of adherence to antihypertensive drugs and oral antidiabetic drugs/insulin, respectively.	Better health-related quality of life was observed in the domains of color vision, driving, and social aspects of the National Eye Institute Visual Functioning Questionnaire. Individuals with lower scores on the National Eye Institute Visual Functioning Questionnaire and higher scores on the Morisky Scale were more likely to be non-adherent to diabetes and hypertension medications.

Visual stability in diabetic retinopathy treated by laser panphotocoagulation	Jr; Takahashi; Bonnomy; Marback; Kara-Jose, 2007	To evaluate the effect of laser therapy on visual acuity in patients with advanced diabetic retinopathy without visual complaints.	The sample consisted of 44 patients, totaling 67 eyes, of which 37 (55.2%) had proliferative diabetic retinopathy and 30 (44.8%) had severe or very severe non-proliferative retinopathy. Pre-treatment visual acuity ranged from 0.5 to 1.0 (mean 0.83 ± 0.17). There was no statistically significant change in visual acuity (p= 0.057) before and after treatment during the study period.	There was visual stability after treatment with panphotocoagulation, which emphasizes the need for interventions in earlier stages of diabetic retinopathy to preserve visual function.
Prevalence of diabetes and diabetic retinopathy in the Brazilian population	SCHELLINI; CARVALHO; RENDEIRO; PADUANS; HIRAI, 2014	OBJECTIVE: To evaluate the prevalence of type 2 diabetes mellitus and diabetic retinopathy (DR) in a Brazilian population.	The prevalence of type 2 diabetes was 8.68% (95% confidence interval, CI, 7.87-9.48%), and DR was present in 7.62% (95% CI 5.02-10.20%) of participants with self-reported type 2 diabetes. . Approximately 35.4% of individuals diagnosed with DR did not know they had diabetes prior to DR diagnosis. The prevalences of low vision and blindness were higher among those with diabetes and DR. Cataracts were still one of the leading causes of blindness in this population.	This is the first large population-based study on HR in Brazil. High rates of visual impairment have been found in people with type 2 diabetes, but cataracts are still a leading cause of blindness. Major surveys are needed to advocate for public health policies in developing countries.
Novel Antihyperglycemic Agents for Type 2 Diabetes and Their Effects on Diabetic Retinopathy	SAW; WONG; HO; LIEW, 2019	With the global increase in rates of type 2 diabetes and complications such as diabetic retinopathy, it is important for ophthalmologists to be aware of these new agents and their impacts on diabetic retinopathy and diabetic macular edema	Our review of the current literature found that, in addition to thiazolidinediones, antihyperglycemic agents have been reported to have beneficial or neutral effects on diabetic ocular complications. Thiazolidinediones (pioglitazone is the only one currently available) have been associated with incident or worsening of diabetic macular oedema, although the rate is believed to be low	Further studies need to be conducted to identify whether the reported beneficial effects are independent of the impact of glycemic control. Early worsening of retinopathy with tight glycaemic control should also be noted when interpreting future studies.

Comparing the Impact of Serum GPER-1 and Oxidant/Antioxidant Levels on Retinopathy in Diabetic Patients and in Healthy Subjects: A Pilot Study	BEYOGLU; Kumar; KASSA; CHRISTENSEN; MEşEN, 2022	This research sought to determine the impact of serum G protein levels on the development of retinopathy in diabetic patients by comparing them to healthy individuals.	A significant difference was found between all groups in terms of serum G protein, oxidant/antioxidant, and estradiol levels ($p<0.01$), but no significant difference was found in terms of thyroid-released hormone or progesterone ($p=0.496$, $p=0.220$, respectively). In the post hoc analysis of the groups with statistically significant differences, another significant difference was found between all groups for serum G protein and oxidant/antioxidant levels ($p<0.05$). Serum G protein levels and oxidant levels were positively correlated, while serum G protein levels and antioxidant levels were negatively correlated ($r=0.622/p<0.01$, $r=0.453/p<0.01$, $r=0.460/p<0.01$, respectively). Multiple regression analysis has shown that increasing serum G protein may help prevent diabetic retinopathy.	Serum G protein levels, which were higher in the diabetic retinopathy group, increased as the oxidant/antioxidant balance shifted in favor of oxidative stress. This appears to be a defense mechanism to prevent neuronal damage.

Source: Authorship

The management of retinal diseases, such as diabetic retinopathy, is a challenge that involves both ophthalmology and endocrinology. Diabetic retinopathy is a microvascular complication of diabetes that can lead to vision loss if not properly managed. Endocrinology plays a crucial role in glycemic control, which is critical in slowing the progression of diabetic retinopathy. In addition, it is also involved in the management of other systemic risk factors, such as hypertension and dyslipidemia, which can accelerate the progression of diabetic retinopathy.

On the other hand, ophthalmology is responsible for regular monitoring of the retina through eye exams and the treatment of eye complications of diabetes. This may include therapies such as laser photocoagulation, intravitreal injection of anti-VEGF drugs, and vitrectomy in advanced cases.

The discussion on the management of diabetic retinopathy involves a careful analysis of the available therapeutic strategies, Mohamed et al. (2007) highlight the importance of glycemic control and early detection of the disease to reduce the risk of visual complications in patients

with diabetes. The proposed approach highlights the need for regular ophthalmologic follow-up for the effective management of diabetic retinopathy.

On another spectrum, Kataoka et al. (2023) investigate the role of fenofibrate in the treatment of diabetic retinopathy. And their results suggest that fenofibrate may be a relevant therapeutic option in preventing disease progression in diabetic patients. Fenofibrate is a drug for dyslipidemia, however, it has been shown to have positive presentations in reducing the progression of diabetic retinopathy in patients with type 2 diabetes. Similarly, semaglutide, an antidiabetic drug, has been associated with a lower risk of diabetic retinopathy in patients with type 2 diabetes. However, it should be considered that there is a need for more research to confirm the efficacy of these drugs and determine their long-term safety profile.

Wang et al. (2021) present important considerations on the potential effect of semaglutide, a GLP-1 receptor agonist, in reducing the risk of diabetic retinopathy in patients with type 2 diabetes. Their randomized controlled trials highlighted the importance of considering not only glycemic control but also other pharmacological interventions in the management of diabetic retinopathy. Since, in addition to the glycemic index, other complications related to diabetes may be associated, such as: arterial hypertension that causes hemorrhage and extravasation of fluids in the retina; high levels of lipids in the blood, in this case, high cholesterol and triglyceride levels can contribute to the development and progression of diabetic retinopathy; Smoking aggravates damage to retinal blood vessels in people with diabetes, increasing the risk of diabetic retinopathy. Genetic susceptibility may play a role in the development of diabetic retinopathy; Pregnant women with diabetes have an increased risk of diabetic retinopathy, especially if they have difficulty controlling their blood glucose levels during pregnancy; Kidney disease and sickle cell anemia can increase the risk of diabetic retinopathy.

It should be noted that it is important to remember that proper diabetes management, along with healthy lifestyle habits such as a balanced diet, regular exercise, and abstaining from smoking, can help reduce the risk and slow the progression of diabetic retinopathy.

In the context of clinical practice, it is essential to consider not only the effectiveness of therapeutic interventions, but also the outcomes related to patients' quality of life. Silva et al. (2005) address patients' perceptions of diabetic retinopathy treatment, highlighting the importance of effective communication between healthcare professionals and patients to ensure treatment adherence and patient satisfaction. The study by Gunay et al. (2024) investigated the relationship between the results of anti-VEGF management on the first day and long-term

outcomes in patients with macular edema due to vascular diseases. These findings provided important information about the efficacy and predictability of anti-VEGF treatment in the management of macular edema, a common complication of diabetic retinopathy.

Jannuzzi et al. (2014) highlight the importance of medication adherence in the context of diabetic retinopathy, especially among the elderly. The quality of life of these patients is intrinsically linked to their ability to adhere to the prescribed treatment, which can significantly influence the course of the disease. The study found that the majority of patients (58%) reported using 80% or more of the prescribed dose and caution when using the medication.

Schellini et al. (2014) provide epidemiological data on the prevalence of diabetes and diabetic retinopathy in a Brazilian population. This information is essential to understand the magnitude of the problem and guide public health policies aimed at the prevention and treatment of the disease. The study found that the prevalence of type 2 diabetes was 8.68% and diabetic retinopathy was present in 7.62% of participants with self-reported type 2 diabetes. This is significantly worrisome, since in addition to the problem involving type 2 diabetes in relation to neuropathies, retinopathy being prevalent causes even more concerns, since not everyone who participated in the study always has knowledge about visual acuity.

Novel antihyperglycemic agents, as discussed by Saw et al. (2019), present opportunities regarding the management of diabetic retinopathy. Evaluating the effects of these agents on disease progression is crucial to determine their long-term efficacy and safety. The review also pointed out that, except for thiazolidinediones, antihyperglycemic agents were reported to have beneficial or neutral effects on diabetic ocular complications.

Finally, the study by Beyoğlu et al. (2022) investigates the effects of serum GPER-1 and antioxidant levels on diabetic retinopathy. These findings have provided relevant considerations about the mechanisms underlying the disease and may lead to the development of new therapeutic strategies. This pilot study was developed in order to compare the effects of serum GPER-1 and oxidant/antioxidant levels on retinopathy in patients with diabetes and healthy individuals. The study found that serum GPER-1 levels, which were higher in the diabetic retinopathy group, increased as the oxidant/antioxidant balance shifted in favor of oxidative stress. This appears to be a defense mechanism to prevent neuronal damage.

Taken together, these studies highlight the complexity of managing diabetic retinopathy and the importance of an approach that unites ophthalmology and endocrinology to provide comprehensive, personalized care to patients with diabetes. More research is needed to continue

advancing the field and improve clinical and quality of life outcomes for this at-risk patient population.

FINAL THOUGHTS

Management of retinal diseases is crucial for preserving visual health and avoiding serious complications, especially in cases such as diabetic retinopathy. The retina is a vital part of the eye, responsible for capturing light and transmitting visual information to the brain. Diseases such as diabetic retinopathy can cause significant damage to the retina, leading to vision loss if not treated properly.

In diabetic retinopathy, controlling blood glucose levels is critical to prevent damage to the retina. However, even with good glycemic control, some patients may still develop retinal complications that require ophthalmic intervention. This is where the therapeutic association between ophthalmology and endocrinology in the treatment of diabetic retinopathy comes in.

Ophthalmology plays the role of diagnosing and treating the complications of diabetic retinopathy. Techniques such as laser photocoagulation, intravitreal drug injections, and vitreoretinal surgery are often used to treat diabetic macular edema, neovascularization, and other manifestations of the disease.

Endocrinology, on the other hand, focuses on the metabolic control of diabetes, aiming to keep glucose levels within a safe range to prevent retinal damage and other micro- and macrovascular complications of the disease. Endocrinology also plays an important role in the management of other diabetes-related conditions that can affect eye health, such as high blood pressure and dyslipidemia.

Collaboration between ophthalmologists and endocrinologists is essential to ensure effective treatment of diabetic retinopathy. This includes addressing both the ophthalmological and endocrinological aspects of the disease, with a view to preserving vision and improving the quality of life of affected patients. Ultimately, this cooperation results in improved clinical outcomes and more effective management of diabetic retinopathy.

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