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Hyperthyroidism and Graves' Disease: Ophthalmological Manifestations and Surgical Treatment.

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LITERATURE REVIEW

RESUMO

Introdução: O hipertireoidismo, caracterizado pela produção excessiva de hormônios pela glândula tireoide, pode levar a várias complicações sistêmicas, incluindo manifestações oftalmológicas, como a Orbitopatia de Graves (OG). A Doença de Graves, uma das principais causas de hipertireoidismo, frequentemente se associa a essas complicações oculares, que incluem protrusão ocular, diplopia e inchaço periocular. O tratamento cirúrgico, incluindo a tireoidectomia total ou subtotal, surge como uma opção para controlar a progressão do hipertireoidismo e melhorar os sintomas oftalmológicos associados. Objetivo: analisar as manifestações oftalmológicas do hipertireoidismo e da Doença de Graves, assim como avaliar a eficácia do tratamento cirúrgico no manejo dessas complicações. Metodologia: A revisão seguiu o checklist PRISMA para garantir rigor e transparência. Foram realizadas buscas nas bases de dados PubMed, Scielo e Web of Science, utilizando cinco descritores: "Hipertireoidismo", "Doença de Graves", "Orbitopatia de Graves", "Tratamento Cirúrgico" e "Manifestações Oftalmológicas". Os critérios de inclusão abrangeram artigos publicados nos últimos 10 anos, estudos focados em tratamento cirúrgico para OG e trabalhos que abordassem explicitamente as manifestações oftalmológicas da Doença de Graves. Foram excluídos estudos que não discutissem o tratamento cirúrgico, artigos não revisados por pares e publicações anteriores a uma década. Resultados: A análise revelou que a Orbitopatia de Graves frequentemente se manifesta por sintomas como protrusão ocular, diplopia e edema periocular, com impacto significativo na qualidade de vida dos pacientes. A tireoidectomia demonstrou ser eficaz na redução dos níveis hormonais, resultando em melhorias sintomáticas para muitos pacientes. No entanto, os resultados variaram, e a abordagem cirúrgica não foi sempre associada a uma resolução completa das manifestações oftalmológicas. Conclusão: O tratamento cirúrgico do hipertireoidismo e da Doença de Graves pode proporcionar alívio significativo das manifestações oftalmológicas, embora não garanta a resolução completa dos sintomas. A cirurgia deve ser considerada em um contexto multidisciplinar, levando em conta a gravidade dos sintomas oculares e a resposta ao tratamento conservador. A revisão destacou a necessidade de estratégias de tratamento integradas para otimizar os resultados para pacientes com

complicações oftalmológicas associadas ao hipertireoidismo e à Doença de Graves.

Palavras-chaves:"Hipertireoidismo", "Doença de Graves", "Orbitopatia de Graves", "Tratamento Cirúrgico" e "Manifestações Oftalmológicas".

ABSTRACT

Introduction: Hyperthyroidism, characterized by the excessive production of hormones by the thyroid gland, can lead to various systemic complications, including ophthalmological manifestations such as Graves' Orbitopathy (GO). Graves' Disease, one of the main causes of hyperthyroidism, is often associated with these ocular complications, which include ocular protrusion, diplopia, and periorbital swelling. Surgical treatment, including total or subtotal thyroidectomy, emerges as an option to control the progression of hyperthyroidism and improve associated ophthalmological symptoms. **Objective**: To analyze the ophthalmological manifestations of hyperthyroidism and Graves' Disease, as well as evaluate the effectiveness of surgical treatment in managing these complications. **Methodology**: The review followed the PRISMA checklist to ensure rigor and transparency. Searches were conducted in PubMed, Scielo, and Web of Science databases using five descriptors: "Hyperthyroidism," "Graves' Disease," "Graves' Orbitopathy," "Surgical Treatment," and "Ophthalmological Manifestations." Inclusion criteria encompassed articles published in the last 10 years, studies focused on surgical treatment for GO, and works explicitly addressing the ophthalmological manifestations of Graves' Disease. Exclusion criteria included studies that did not discuss surgical treatment, non-peer-reviewed articles, and publications older than a decade. **Results**: The analysis revealed that Graves' Orbitopathy frequently manifests with symptoms such as ocular protrusion, diplopia, and periorbital edema, significantly impacting patients' quality of life. Thyroidectomy proved effective in reducing hormone levels, resulting in symptomatic improvements for many patients. However, outcomes varied, and surgical intervention was not always associated with complete resolution of ophthalmological manifestations. **Conclusion**: Surgical treatment of hyperthyroidism and Graves' Disease can provide significant relief from ophthalmological manifestations, though it does not guarantee complete resolution of symptoms. Surgery should be considered within a multidisciplinary context, taking into account the severity of ocular symptoms and response to conservative treatment. The review highlighted the need for integrated treatment strategies to optimize outcomes for patients with ophthalmological complications associated with hyperthyroidism and Graves' Disease.

Keywords: "Hyperthyroidism," "Graves' Disease," "Graves' Orbitopathy," "Surgical Treatment," and "Ophthalmological Manifestations."

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INTRODUCTION:

Graves' Disease is an autoimmune condition that results in hyperthyroidism, characterized by the excessive production of hormones by the thyroid gland. This disease can cause a range of significant ophthalmological complications, known as Graves' Orbitopathy. Ocular protrusion, or exophthalmos, is one of the most visible and troubling manifestations, leading to the enlargement of tissues around the eyes and the forward displacement of the eyeballs. This phenomenon results in an aesthetic alteration that can be distressing for patients, negatively impacting their self-image and social interaction.

In addition to ocular protrusion, Graves' Disease is frequently associated with diplopia, or double vision. This symptom occurs due to the impairment of the eye muscles, which are affected by inflammation and hypertrophy caused by the disease. Diplopia can hinder daily activities such as reading and driving, causing significant discomfort to individuals. These ophthalmological manifestations not only affect visual functionality but also have a profound impact on patients' quality of life. The difficulty in performing daily tasks and the aesthetic discomfort are issues that affect patients' mental and emotional health, making the effective management of these symptoms a priority in the treatment of Graves' Disease.

Surgical treatment emerges as a crucial alternative for managing hyperthyroidism and its associated ophthalmological complications in Graves' Disease. Thyroidectomy, which can be performed in total or subtotal form, is often indicated for patients with severe or treatment-resistant hyperthyroidism. The main objective is to reduce thyroid hormone production to normal levels, which can help alleviate ocular symptoms and improve quality of life.

However, the effectiveness of surgical treatment varies among patients. Although the intervention can lead to a significant reduction in hormone levels and consequently improve ocular symptoms, it does not guarantee the complete resolution of ophthalmological manifestations. Some patients may continue to experience symptoms such as ocular protrusion and diplopia even after surgery, requiring ongoing monitoring and, in some cases, additional interventions.

Given the complex impact of Graves' Disease and its complications, a multidisciplinary approach is essential to optimize treatment. Collaboration between endocrinologists, ophthalmologists, and surgeons is crucial to providing comprehensive and coordinated care. This integration allows for effective management of the different dimensions of the disease, ensuring that both hormonal and ophthalmological aspects are appropriately and integratively treated. Thus, the successful treatment of Graves' Disease requires a collaborative strategy that meets the individual needs of each patient.

The systematic literature review aims to thoroughly examine the ophthalmological manifestations associated with hyperthyroidism and Graves' Disease, evaluating the effectiveness of various surgical treatments available. It intends to analyze how total or subtotal thyroidectomy and other surgical approaches influence the reduction of ocular symptoms, including ocular protrusion and diplopia. Additionally, the review seeks to identify factors that contribute to the success or failure of these treatments and to assess the impact of a multidisciplinary approach, involving endocrinologists, ophthalmologists, and surgeons, on the effective management of Graves' Disease. The goal is to provide a comprehensive view of the best practices and strategies to optimize the treatment of ophthalmological complications associated with hyperthyroidism.

METHODOLOGY

The methodology adopted for this systematic literature review strictly followed the PRISMA checklist, ensuring transparency and consistency in data analysis. Searches were conducted in the PubMed, Scielo, and Web of Science databases using the descriptors "Hyperthyroidism," "Graves' Disease," "Graves' Orbitopathy," "Surgical Treatment," and "Ophthalmological Manifestations." This approach ensured the necessary breadth and depth to identify and select relevant studies on the topic.

The inclusion criteria established were as follows: studies published in the last 10 years, ensuring the currency of the information; articles explicitly focusing on the surgical treatment of hyperthyroidism and its ophthalmological implications; works that detailed the ophthalmological manifestations associated with Graves' Disease; peer-reviewed research, ensuring data quality and credibility; studies providing quantitative

or qualitative data on the effects of surgery in improving ocular symptoms.

The exclusion criteria included: studies published before the last 10 years to ensure the current relevance of the information; articles that did not discuss the relationship between surgical treatment and ophthalmological manifestations, limiting the review's focus; works not peer-reviewed, compromising data integrity; studies that only addressed theoretical or speculative aspects without empirical data; publications that did not present a clear analysis of surgical treatment outcomes on the ophthalmological manifestations of Graves' Disease.

The selection of works followed a meticulous screening process, including the reading of abstracts and the analysis of complete texts to ensure adherence to established criteria. Data collection and analysis were conducted with attention to methodological details, ensuring that all included studies contributed significantly to understanding the ophthalmological manifestations and the effectiveness of surgical treatment in Graves' Disease.

RESULTS

Fifteen articles were selected Graves' Disease is an autoimmune condition that results in hyperthyroidism and frequently triggers notable ophthalmological manifestations. Among these manifestations, ocular protrusion, known as exophthalmos, is one of the most prominent. This symptom occurs due to the infiltration of inflammatory cells and increased tissue volume around the eyeballs. The limited space within the ocular orbit causes the tissue expansion to exert pressure on the eyeballs, pushing them forward and causing protrusion. This condition can lead to a visible aesthetic alteration and significant discomfort, directly affecting patients' appearance and self-esteem.

In addition to ocular protrusion, diplopia, or double vision, is another relevant ophthalmological manifestation associated with Graves' Disease. Diplopia results from changes in the function of the extraocular muscles, which become inflamed and hypertrophied due to the autoimmune process. This condition impairs the coordination of the eye muscles, hindering the patient's ability to focus on objects clearly and causing double vision that interferes with daily activities. The combination of ocular protrusion

and diplopia impairs visual functionality and can lead to difficulties in tasks such as reading and driving, contributing to an overall reduction in quality of life.

The impact of ophthalmological manifestations of Graves' Disease is profound and multifaceted. Firstly, ocular protrusion and diplopia can have a significant effect on patients' self-image. The change in facial appearance caused by ocular protrusion can lead to emotional discomfort and negative psychological impact. Difficulty in performing daily activities, such as working or socializing, due to diplopia also contributes to a deterioration in quality of life. Additionally, ophthalmological symptoms may necessitate medical and surgical interventions, adding another layer of complexity to the management of Graves' Disease.

Moreover, the consequences of these ophthalmological manifestations affect not only the emotional sphere but also the practical functionality of patients. The inability to effectively perform daily tasks can lead to a reduction in work capacity and engagement in social activities. This functional impact intensifies the stress and anxiety associated with the condition, creating a cycle of adverse effects that requires a comprehensive therapeutic approach. Therefore, effective management of these ophthalmological manifestations is essential for improving patients' quality of life and mitigating the negative effects associated with Graves' Disease.

Pharmacological treatment of hyperthyroidism, a condition frequently associated with Graves' Disease, is a central strategy in disease management and minimizing ophthalmological manifestations. Antithyroid medications, such as methimazole and propylthiouracil, play a crucial role in regulating thyroid hormone levels. These drugs work by inhibiting the synthesis of thyroid hormones, leading to reduced levels of T3 and T4 in the body. Normalizing these hormones helps alleviate symptoms associated with hyperthyroidism, including those affecting ocular function. Consequently, proper and continuous administration of these medications can significantly contribute to the improvement of ophthalmological symptoms associated with Graves' Disease.

In addition to antithyroid medications, treatment may include the use of beta-blockers, which help control cardiovascular and systemic symptoms of hyperthyroidism, such as tachycardia and tremors. While these medications do not have a direct effect on

ophthalmological manifestations, they help control the overall disease burden, which can indirectly and positively impact ocular symptoms. The combination of therapies, therefore, provides a more comprehensive treatment approach, addressing both hormonal and systemic aspects of hyperthyroidism. Thus, the use of a well-planned and monitored pharmacological approach is essential for the effective management of Graves' Disease and its ophthalmological complications.

Thyroidectomy represents a significant surgical approach in the treatment of hyperthyroidism and the management of ophthalmological manifestations associated with Graves' Disease. This intervention can be performed in total or subtotal form, depending on the severity of the condition and the specific needs of the patient. The main purpose of thyroidectomy is to reduce thyroid hormone production, which, when excessive, contributes to the worsening of ocular symptoms. Surgical removal of thyroid tissue can lead to significant improvement in hormonal function, which, in turn, may alleviate the severity of ocular symptoms, such as ocular protrusion and diplopia.

However, the effectiveness of thyroidectomy can vary among patients and does not always result in a complete resolution of ophthalmological symptoms. Although hormonal reduction may provide relief from ocular symptoms, some patients may continue to experience ocular protrusion and diplopia even after surgery. This is because ophthalmological manifestations may be partially independent of hormonal levels and more related to structural changes in the ocular orbit. Therefore, post-surgery, additional follow-up and, in some cases, further treatments may be necessary to fully address persistent ophthalmological complications. The integration of surgical approaches with complementary treatment strategies is, therefore, crucial for achieving the best possible clinical outcomes.

Surgical treatment for Graves' Orbitopathy, a common ophthalmological complication in Graves' Disease, constitutes a vital approach to relieving associated symptoms. Orbital decompression is a specific surgical procedure performed to reduce intraorbital pressure and consequently improve ocular protrusion. This treatment involves removing part of the orbital bones and, in some cases, adjacent soft tissues, to create more space within the ocular orbit. Creating this additional space helps accommodate the increased inflammatory tissue and reduces pressure on the eyeballs,

alleviating symptoms such as exophthalmos and diplopia.

Furthermore, surgery for Graves' Orbitopathy may include correction of the extraocular muscles, which are often involved in the inflammatory process. The surgical approach to the extraocular muscles aims to correct ocular deviations and restore eye motor function, which can significantly improve double vision. Combining orbital decompression with extraocular muscle correction allows for a comprehensive approach to treating ophthalmological complications, providing symptom relief and improving patients' quality of life. Therefore, the effectiveness of this surgical treatment depends on the precision of the procedure and the appropriate selection of patients who would benefit most from the intervention.

A multidisciplinary approach in managing Graves' Disease, particularly when considering the combination of hyperthyroidism and ophthalmological manifestations, is essential for achieving optimal clinical outcomes. Effective treatment of this complex condition often requires collaboration among endocrinologists, ophthalmologists, and surgeons. Each specialty provides a unique perspective and set of skills to address both hormonal aspects and ocular complications. Endocrinologists are responsible for controlling hormone levels and managing hyperthyroidism through pharmacological therapies and, when necessary, surgical interventions on the thyroid gland.

Ophthalmologists, in turn, focus on treating the specific ophthalmological complications of Graves' Disease, such as ocular protrusion and diplopia. They conduct detailed assessments of ocular function and offer therapeutic options for symptom relief, including recommending surgery for orbital decompression or extraocular muscle correction. Surgeons may perform procedures for both controlling hyperthyroidism and correcting ophthalmological complications. The integration of these specialties is crucial for comprehensive and coordinated management, addressing all dimensions of Graves' Disease and its clinical implications.

Evaluating the effectiveness of surgical treatment in Graves' Disease is a critical aspect of ensuring that the interventions produce the desired results. Following procedures such as thyroidectomy or orbital decompression, close monitoring of patients' clinical responses is necessary. Effectiveness is assessed based on improvement in ophthalmological symptoms, such as reduced ocular protrusion and

correction of diplopia. Additionally, the impact on thyroid function is a crucial success criterion. Results analysis should consider both clinical benefits achieved and any possible complications or adverse effects that may arise after surgery.

Continuous monitoring after surgical treatment involves regular evaluations to adjust therapy and address any potential complications. This may include conducting follow-up ophthalmological examinations to assess patients' responses to surgery and adjust the treatment plan as needed. The effectiveness of surgical treatment should be reviewed continuously, taking into account both symptom improvement and overall quality of life. Therefore, systematic evaluation of postoperative outcomes and adjustment of treatment are essential to ensure the best therapeutic approach and maximize benefits for patients with Graves' Disease.

Preventing ophthalmological complications in patients with Graves' Disease is a crucial aspect of managing the condition. Effective preventive strategies can minimize symptom severity and improve patients' quality of life. Initially, early identification and treatment of hyperthyroidism are key to preventing the progression of ophthalmological complications. Implementing appropriate treatments, such as antithyroid medications and regular monitoring of hormone levels, can reduce inflammation and swelling of the orbital tissues, which are contributing factors to the disease's ocular manifestations.

Furthermore, proactive disease management includes educating patients about risk factors associated with the progression of ophthalmological symptoms. Patients should be informed about the importance of avoiding factors that may exacerbate the condition, such as prolonged sun exposure and smoking, which has been associated with worsening ophthalmological manifestations. Adopting preventive measures, such as using protective eyewear and maintaining healthy habits, can play a significant role in reducing the risk of complications. Thus, implementing preventive strategies helps limit the severity of ophthalmological complications and contributes to a better long-term prognosis.

Ophthalmological rehabilitation is essential for patients with persistent or severe symptoms of Graves' Disease, despite treatment. This multidimensional approach aims to address both functional and aesthetic aspects of ocular manifestations. Rehabilitation may include visual therapy, which helps improve eye coordination and alignment, and

psychological support to cope with the emotional impact of the condition. Additionally, the use of optical devices, such as prism lenses, may be recommended to correct diplopia and enhance the patient's vision.

Another important aspect of ophthalmological rehabilitation is ongoing monitoring and evaluation of treatment results. Regular exams allow for the assessment of intervention effectiveness and adjustment of treatment plans as needed. Collaboration among ophthalmologists, therapists, and other healthcare professionals is crucial to develop and implement an individualized rehabilitation plan that addresses each patient's specific needs. Therefore, effective rehabilitation not only improves visual function but also addresses the psychological and social impact of Graves' Disease.

Research on new therapies and emerging approaches in treating Graves' Disease reflects ongoing advances in the field of endocrinology and ophthalmology. Current investigations are focusing on developing more effective and less invasive methods for managing both hyperthyroidism and associated ophthalmological manifestations. Among these innovations, monoclonal antibody therapy, such as teprotumumab, has gained prominence. This medication specifically targets the inflammatory pathways involved in Graves' Orbitopathy, offering a promising alternative to conventional treatments. The use of these agents may significantly reduce inflammation and

CONCLUSION

The analysis of available data on Graves' Disease and its ophthalmological manifestations reveals significant advancements in understanding and managing the condition. Treatment of Graves' Disease, focusing on controlling hyperthyroidism and associated ocular complications, has demonstrated that therapeutic approaches must be integrated and personalized to achieve the best outcomes. Scientific studies have confirmed that antithyroid therapy remains an effective approach for controlling hormone levels, while thyroidectomy has shown significant benefits in refractory cases.

Regarding ophthalmological complications, orbital decompression has emerged as a crucial solution for relieving ocular protrusion and improving patients' quality of life. Correction of the extraocular muscles has also proven effective in reducing

diplopia. The combination of these surgical interventions, along with new therapies such as monoclonal antibody use, provides a more comprehensive and targeted treatment.**

Research into emerging approaches has expanded the available therapeutic options, showing that new technologies and innovative treatments have the potential to significantly improve prognosis for patients with Graves' Disease. The use of advanced imaging techniques and specific therapies reflects the ongoing evolution in disease management, allowing for more effective and personalized treatments.

Therefore, the current approach to Graves' Disease should consider both the treatment of hyperthyroidism and the management of ophthalmological manifestations. Integrating traditional and emerging strategies provides substantial improvement in treatment and patient well-being, highlighting the importance of a multidisciplinary approach tailored to individual needs.

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