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INTERCONNECTIONS BETWEEN ERECTILE DYSFUNCTION AND METABOLIC DISEASES: AN INTEGRATIVE ANALYSIS

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Abstract: Objective: To evaluate the relationship between erectile dysfunction (ED) and metabolic diseases, exploring how metabolic factors affect the occurrence of ED. Methodology: Using PVO approach, the search was conducted in the PubMed Central database. The initial selection of 44 articles was refined to14after applying the inclusion and exclusion criteria. Studies have highlighted a two-way interaction between prediabetes/type 2 diabetes (T2D) and ED, with testosterone deficiency as a common factor. Revision: Identifying ED using the International Index of Erectile Function-5 (IIEF-5) is vital for effective treatment. Therapeutic strategies include phosphodiesterase type 5 inhibitors, hormonal therapy and lifestyle changes aimed at improving erectile function and metabolic and cardiovascular control. Final Considerations: This review emphasizes the importance of additional research to elucidate the complex interactions between ED and metabolic conditions. An integrated treatment, considering endocrinological aspects, glycemic control and cardiovascular risk factors, is crucial to improving clinical results and patients' quality of life.
Keywords: Erectile Dysfunction, Metabolic Diseases, Glycemic Control.

INTRODUCTION

The intersection between diabetes mellitus (DM) and erectile dysfunction (ED) has attracted considerable attention in the medical community due to the increasing prevalence of both conditions and the significant impact they have on patients' quality of life. Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia resulting from problems in the metabolism of carbohydrates, fats and proteins. The condition is bifurcated into two main types: type 1 diabetes mellitus (T1D), an autoimmune disease that results in the destruction of the insulin-producing

beta cells of the pancreas, and type 2 diabetes mellitus (T2D), often associated with metabolic syndrome and insulin resistance (Ghanem et al., 2021).

DM2, in particular, is a globally prevalent condition, with projections indicating an increase in incidence, reaching an expected 642 million affected individuals by 2040. Chronic hyperglycemia and metabolic syndrome associated with DM2 contribute to a variety of harms and dysfunctions in multiple organs, facilitating the development of micro and macrovascular complications, including erectile dysfunction (Ghanem et al., 2021).

Erectile dysfunction, defined as the inability to maintain a penile erection sufficient for sexual satisfaction, affects approximately 100 million men globally.

This multifactorial disorder is influenced by neurological and vascular components, and by the mechanism of veno-occlusion and relaxation of the trabecular muscles. The prevalence of ED is on the rise and is expected to continue increasing, reaching approximately 322 million cases by 2025, which represents a substantial challenge for public health (Aleksandra; Aleksandra; Iwona, 2022; Xiong et al., 2024; Parmar et al., 2022).

The complexity of the relationship between DM2 and ED is marked by the interaction of pathophysiological, hormonal and metabolic factors. Studies indicate that ED in patients with metabolic syndrome may be a consequence of several mechanisms, including diabetic microangiopathy, somatic and autonomic neuropathies, hormonal dysregulation and insulin resistance. These factors contribute to a pro-inflammatory state and endothelial dysfunction, exacerbating the erectile condition (Aleksandra; Aleksandra; Iwona, 2022; Yilmaz et al., 2021).

Additionally, increased visceral adiposity is associated with high expression of aromatase, an enzyme that converts testosterone into estradiol, resulting in subnormal testosterone levels and contributing to the pathogenesis of ED. Certain medications frequently prescribed for patients with T2DM have also been implicated as factors in the development of sexual impotence in patients (Ghanem et al., 2021; Aleksandra; Aleksandra; Iwona, 2022).

This literature review aims to explore the complex relationship between erectile dysfunction and metabolic diseases, evaluating how metabolic factors influence the occurrence of erectile dysfunction, with a particular focus on the challenges and opportunities to improve clinical outcomes and patients' quality of life.

METHODOLOGY

This bibliographic review was designed following the pvo approach, adjusted to analyze the relationship between erectile dysfunction and metabolic diseases in patients. The central question explored was: "What is the impact of metabolic diseases on the incidence of erectile dysfunction inpatients, and how can these findings guide effective interventions and treatments?"

The search was carried out in the PubMed Central (PMC) database. The descriptors used were "Erectile dysfunction", "Metabolic syndrome", "Diabetes Mellitus", and "Association", combined using the Boolean operator "AND". The initial search resulted in 170 articles.

The inclusion criteria adopted for the selection of articles were: works in English and Portuguese, published between 2019 and 2024, that addressed topics relevant to the research, including systematic reviews and meta-analyses, all available in full. Exclusion criteria included: publications available only

in abstract form, and those that did not directly address the research question or that did not meet the other inclusion criteria.

After rigorous application of the selection criteria, they were chosen14articles to compose the final corpus of this review. These articles were analyzed to better understand the association between erectile dysfunction and metabolic diseases, with the aim of identifying guidelines for more effective treatment and intervention in this population. This methodology allowed for a comprehensive and up-to-date assessment of the available literature, offering a solid basis for understanding the complex interactions between erectile dysfunction and metabolic conditions, aiming to improve the quality of life of affected patients.

DISCUSSION

PATHOPHYSIOLOGICAL MECHANISMS OF ERECTILE DYSFUNCTION IN METABOLIC DISEASES

To understand the relationship between ED and metabolic disorders, it is essential to analyze the pathophysiological mechanisms involved. A study by Tucker, Salas, Secrest, and Scherrer (2023) observed a bidirectional association between prediabetes/type 2 diabetes mellitus and ED, suggesting testosterone deficiency as a common link between these conditions. Testosterone deficiency is often associated with obesity, insulin resistance and depression, factors that contribute to the deterioration of micro- and macrovascular systems and neuropathies (Tucker et al., 2023; Mazzilli et al., 2022).

The factors involved in the development of ED are varied and include vasculopathy, neuropathy and hormonal changes such as androgen depression. Specifically, diabetic autonomic neuropathy adversely affects the autonomic nervous system, interfering with penile tumescence and rigidity. The underlying mechanism involves deterioration of non-adrenergic and non-cholinergic nerve endings and an alteration in the release of nitric oxide, essential for normal erectile function (Agochukwu-Mmonu et al., 2020).

Yuan et al. (2021) highlight that the pathophysiological mechanisms of ED also involve microvascular damage that leads to tissue hypoxia and endothelial dysfunction induced by an increase in reactive oxygen species. These factors are vital to understanding how diabetic complications exacerbate ED.

An additional prospective, observational study investigated the relationship between ED severity and pupillary functions in diabetic patients, finding that changes in static and dynamic pupillometry are indicative of diabetic autonomic neuropathy, which can directly affect erectile function. This condition emphasizes that ED in diabetic patients can be exacerbated by autonomic dysfunction, which affects relaxation of the corpus cavernosum smooth muscle essential for erection. However, the authors emphasize that ED must not be attributed exclusively to neuropathy, as tissue changes are also relevant, although the severity of neuropathy is a significant factor in the etiology of ED in diabetics (Cankurtaran; Ozates; Ozler, 2019; Agochukwu-Mmonu, Pop-Busui, Wessells & Sarma, 2020).

Testosterone plays a crucial role in regulating the expression of nitric oxide synthase, essential for the vasodilation of penile tissue and regulation of the expression of phosphodiesterase type 5 inhibitors, necessary for the relaxation of muscle cells in the cavernous tissue and maintenance of erection (Mazzilli et al. al., 2022). In contrast, high levels of prolactin can inhibit the release of gonadotropin hormones, decreasing testosterone secretion and, consequently, worsening ED.

A study conducted by Tucker, Salas, Secrest and Scherrer (2023) aimed to evaluate the risk of pre-diabetes and type 2 diabetes mellitus (DM2) among young patients with or without a diagnosis of ED, revealing a bidirectional association between these conditions. A crucial finding was the identification of low testosterone as a common factor linking ED and metabolic syndrome, suggesting that hormonal impairment is a central element in the pathogenesis of ED in metabolic contexts.

Furthermore, cardiovascular diseases (CVD), including coronary artery disease (CAD) and heart failure, are significantly associated with the development of ED. Studies indicate that these conditions can reduce mean arterial pressure, consequently reducing intracavernous pressure, essential for maintaining an erection. Increased phosphorylation of ROCK 2 and MYPT-1, which contributes to cavernous tissue contraction, is also related to CVD and exacerbates ED (Li et al., 2023).

In the context of CVD, a study by Li, Long, Ren, and Bing (2023) examined how CVD contributes to the development of ED, noting a direct relationship between coronary artery disease, heart failure, and the incidence of ED (Li et al., 2023).

A retrospective observational study conducted by Mazzilli et al. (2022) evaluated 1782 patients with ED, demonstrating that individuals with newly diagnosed DM2 have a more severe form of ED compared to the total group. This study highlights that ED can be an early marker of endothelial damage and hyperglycemia, potentially being the first indicator of DM in approximately 12-15% of cases.

Additionally, studies by Yuan et al. (2021) corroborate this connection, highlighting the interaction between vascular, hormonal and neurological events in the pathophysiology of ED. The authors explain that microvascular damage, resulting in tissue hypoxia and insufficient supply to the nerves, along with increased reactive oxygen species induced by hyperglycemia, contribute to endothelial dysfunction and reduced nitric oxide levels. These factors impair the vasodilation necessary for an adequate erection and are closely linked to hypogonadism resulting from low testosterone (Yuan et al., 2021).

Endocrine disorders such as hypogonadism and hyperprolactinemia are strongly associated with ED. Hypogonadism, which manifests with low testosterone levels, is present in about 21% of men with ED. Testosterone is crucial for regulating the expression of nitric oxide synthase, facilitating vasodilation of penile tissue and relaxation of muscle cells in cavernous tissue. High levels of prolactin can inhibit the release of gonadotropins, decreasing testosterone secretion and exacerbating erectile dysfunction (Mazzilli et al., 2022).

INTEGRATED DIAGNOSIS AND TREATMENT APPROACHES FOR ERECTILE DYSFUNCTION IN PATIENTS WITH METABOLIC DISEASES

The diagnosis of ED in patients with metabolic diseases, such as DM, is crucial for effective management and improving the quality of life of those affected. The assessment of ED can be carried out using the International Index of Erectile Function-5 (IIEF-5), which considers variables such as age, BMI, family history of DM, duration of diabetes, smoking habits, physical activity, comorbidities, and levels of lipids and blood glucose (Defeudis et al., 2022). This tool is instrumental in correlating ED with underlying metabolic pathologies.

The treatment of ED in patients with DM2 is complex due to the interconnection of these conditions with oxidative stress

and the reduction in the bioavailability of endothelial nitric oxide (Li et al., 2020). Studies indicate that metformin can improve erectile function in diabetic patients, as demonstrated by significant improvements in IIEF score after treatment (Defeudis et al., 2022). Furthermore, the combination of therapies such as liraglutide with testosterone and metformin has shown promising results, suggesting that combination treatments may be more effective than isolated approaches.

A relevant aspect in ED therapy is the administration of PDE5i. Studies demonstrate that early and increased use of PDE5i can quickly improve erectile function, reducing the need for diagnoses related to this symptom (Mazzilli et al., 2022). Furthermore, diabetes management and lifestyle modification, including adherence to the Mediterranean diet, have been shown to be beneficial in preserving erectile function, in contrast to Western diets that pose additional risks for ED (Defeudis et al., 2022).

It is equally important to highlight the role of cardiovascular conditions in the development of ED. Patients with coronary artery disease or heart failure often experience ED due to reduced mean arterial pressure, which negatively affects the intracavernous pressure required for adequate erection (Li et al., 2023). This phenomenon reinforces the need for an integrated approach that considers both metabolic control and cardiovascular health.

Regarding hormonal treatment, hypogonadism and hyperprolactinemia are endocrine disorders significantly associated with the development of ED. The regulation of testosterone and control of prolactin levels are essential for maintaining erectile function (Mazzilli et al., 2022).

Finally, integrating nutritional approaches, such as a low-carb diet for patients with metabolic syndrome, may not only improve testosterone levels and erectile function, but also reduce insulin resistance and promote vascular health (Schmitt et al., 2023). Vitamin D supplementation has also been identified as a potential strategy to improve endothelial health and control glycemia in patients with T2DM, opening new perspectives for the treatment of ED (Ariman et al., 2021).

FINAL CONSIDERATIONS

Available information highlights a complex relationship between metabolic diseases and ED, associated with risk factors such as obesity and hypertension. Recent studies highlight the role of vascular, neurological and hormonal mechanisms exacerbated by conditions such as diabetes mellitus and metabolic syndrome. These conditions not only affect erectile function, but also significantly impact patients' mental health and quality of life. There is an urgent need for additional research to explore the specific pathophysiological mechanisms that connect ED to metabolic changes, as well as to evaluate innovative therapies that integrate sexual and metabolic aspects.

An integrated strategy that includes endocrinological, glycemic control and cardiovascular risk management is crucial, as well as innovative treatments such as phosphodiesterase type 5 inhibitors and personalized diets to improve clinical results and patients' quality of life.

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