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POST-GONADECTOMY HORMONE THERAPY IN MORRIS SYNDROME: STRATEGIES TO MINIMIZE SIDE EFFECTS AND MAXIMIZE QUALITY OF LIFE

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ABSTRACT

Morris Syndrome, characterized by androgen insensitivity, requires post-gonadectomy hormone therapy to maintain bone, cardiovascular, and psychological health. The integrative review highlights the importance of transdermal estrogens and clinical monitoring to minimize risks and optimize quality of life.

Keywords: Morris syndrome. Hormone Therapy.

INTRODUCTION

Morris Syndrome, also known as Androgen Insensitivity Syndrome (AIS), is a rare genetic disorder in which individuals with XY carion have a female phenotype due to tissue resistance to androgens (Hughes *et al*., 2019). This condition results in the difference between the chromosomal sex and the external phenotype, leading to the absence of male secondary sex characteristics and the presence of typical female structures such as external genitalia and breast development (Cools *et al*., 2020).

Gonadectomy is often recommended in these cases due to the risk of gonadal neoplasia, which can develop over a lifetime in individuals with retained testicles (Deans *et al*., 2017). However, the removal of the gonads leads to hormone deficiency, which makes it essential to adopt a replacement therapy to minimize the adverse effects of hormone loss (Raisanen *et al*., 2021).

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Hormone therapy is essential to maintain bone and cardiovascular health and quality of life in these patients. Studies indicate that estrogen replacement is essential to avoid osteoporosis and reduce the risk of cardiovascular diseases, in addition to providing psychological well-being and quality of life (Bertelloni & Dati, 2019).

However, adherence to treatment and the choice of the appropriate therapeutic regimen pose clinical challenges, as each patient may respond differently to hormone therapy. In addition, side effects such as mood swings, weight gain, and thromboembolic complications should be monitored carefully (Wisniewski *et al*., 2020).

Therefore, understanding the best strategies to optimize post-gonadectomy hormone therapy in Morris Syndrome is essential to ensure the physical and emotional health of patients while minimizing side effects and maximizing their quality of life.

OBJECTIVE

This study aims to analyze the strategies of post-gonadectomy hormone therapy in Morris Syndrome, discussing their benefits, side effects, and best approaches to promote quality of life and well-being of patients.

METHODOLOGY

This study adopted a qualitative approach with an integrative review of the literature, to analyze the strategies of hormone therapy after gonadectomy in Morris Syndrome. The guiding question that guides this research is: "What are the best strategies to optimize post-gonadectomy hormone therapy in Morris Syndrome, minimizing side effects and maximizing the quality of life of patients?".

Studies published in the last five years in databases such as *PubMed*, *Scopus* and *SciELO* were selected. The descriptors used for the search were: "Morris Syndrome", "Hormonal Therapy", "Gonadectomy", "Quality of Life" and "Therapeutic Strategies". To ensure the quality of the research, only original articles, systematic reviews and meta-analyses that addressed hormone therapy in individuals with Morris Syndrome were included, in addition to clinical studies and pertinent case reports.

The inclusion criteria included studies that dealt with hormone therapy in patients with Morris Syndrome, focusing on the effects of hormone treatment, choice of hormone type, dose, impacts on bone, cardiovascular and psychological health, as well as strategies to minimize adverse effects and promote the well-being of patients. Studies with inadequate methodologies or that did not provide relevant data for the proposed analysis were excluded.

To ensure the reliability of the data, the screening of the articles was carried out independently by two researchers, who evaluated the studies for their methodological quality. The selected articles were organized into thematic categories to facilitate the discussion of the results, focusing on the efficacy of hormone therapy, treatment adherence, adverse effects, and impact on the quality of life of patients.

In addition to the literature review, observational data from clinical studies and case reports were considered to provide a more comprehensive view of therapeutic approaches and their long-term implications. The evaluation of each study followed a critical analysis that included an analysis of the variables involved, such as the type of hormone used, therapeutic regimen, and monitoring of adverse effects.

The data analysis was done qualitatively, allowing the identification of gaps in the literature and providing a basis for the formulation of recommendations for future research and treatment strategies. The study respects the ethical principles of scientific research, ensuring transparency and integrity in the analysis of results. Finally, 11 articles were selected for the present review.

DEVELOPMENT

The reviewed studies indicate that hormone replacement with estrogens plays a key role in maintaining the bone and cardiovascular health of patients. Estrogen deficiency after gonadectomy is strongly associated with increased risk of osteoporosis, metabolic diseases, and other endocrine disorders (Hughes *et al.*, 2019; Wisniewski *et al.*, 2020; Raisanen *et al.*, 2021).

Estrogen is a hormone crucial for the regulation of bone metabolism, and its deficiency can lead to accelerated bone demineralization, increasing women's vulnerability to fractures, especially after menopause or gonad removal surgery. Recent studies have also emphasized the link between estrogen deficiency and the incidence of cardiovascular disease, since the hormone has a protective effect on the cardiovascular system, modulating vascular function and the inflammatory response (Smith *et al.*, 2023).

In addition, the choice of the type of estrogen to be administered is a determining factor in the safety and efficacy of the therapy. Several studies have shown that transdermal estrogens, which are administered through the skin, have a significant advantage over oral formulations in terms of thromboembolic risk. Oral estrogen preparations have been associated with an increased risk of deep vein thrombosis and pulmonary embolism, conditions that are not seen as often in transdermal therapies (Bertelloni & Dati, 2019; García *et al.*, 2022). This difference occurs due to the mode of absorption of estrogens, which, in oral formulations, pass through the

liver before entering the systemic circulation, which can increase the production of coagulation factors. In contrast, transdermal absorption avoids this effect, providing a safer alternative for women with a predisposition to thromboembolic events.

Another critical factor in hormone replacement therapy is the age at which treatment is initiated. Evidence suggests that the early introduction of hormone replacement has a significant impact on long-term bone and cardiovascular health. Women who start hormone replacement soon after estrogen loss, either through natural menopause or surgery, have lower bone mineral density losses and a reduced risk of cardiovascular disease, when compared to those who start therapy late (Wisniewski *et al.*, 2020; Deans *et al.*, 2017). A 2023 study by Thompson *et al.*, reinforced the importance of the early therapeutic window, highlighting that hormone replacement started in the first five years after menopause can minimize the negative effects on the cardiovascular system, particularly on endothelial function and blood pressure regulation.

Hormone therapy also has a significant effect on the psychological well-being of patients. Patients on hormone replacement treatment often report an improvement in self-esteem, quality of life, and overall well-being, particularly about menopausal symptoms such as hot flashes, sleep disturbances, and mood swings (Raisanen *et al.*, 2021). The absence of hormone replacement, on the other hand, has been linked to increased depressive symptoms and anxiety, conditions that may be exacerbated by the abrupt drop in estrogen levels (Kumar *et al.*, 2023). These psychological changes are particularly relevant in women who go through early menopause, either for natural reasons or as a result of surgical interventions such as gonadectomy. Hormone replacement, in these cases, not only improves physical symptoms, but also contributes to emotional and psychological balance, which is essential for the quality of life of patients.

However, despite the evident benefits of hormonal therapy, clinical follow-up should be rigorous and personalized, aiming to adjust therapy according to the individual needs of each patient. Hormone replacement is not without risks and can have side effects, such as weight gain, mood swings, increased cardiovascular risk, and other metabolic problems. Therefore, health professionals must perform continuous monitoring, adjusting the dosage and type of estrogen according to the patient's clinical response (Cools *et al.*, 2020). More recent studies, such as that of Martinez *et al.* (2024), reinforce that regular monitoring of parameters such as blood pressure, lipid profile, and bone density is essential to minimize the risks associated with hormone replacement therapy.

In addition, an integrated and multidisciplinary approach has been increasingly recommended in the management of patients on hormone replacement. Professionals from

different areas, such as endocrinologists, gynecologists, nutritionists, and psychologists, must work together to ensure effective treatment and a more humanized approach. Psychological support is particularly valuable for patients who experience emotional and psychological symptoms during hormone therapy, while genetic counseling can help with personalization of therapy, considering genetic factors that may influence treatment response (Deans *et al.*, 2017; Bertelloni & Dati, 2019). The combination of these complementary approaches has shown additional benefits, promoting adherence to treatment and improving long-term outcomes.

It is important to note that the choice of estrogen type should be made according to the clinical characteristics of each patient, taking into account factors such as medical history, cardiovascular risk, and possible contraindications. Recent studies, such as the one by Yang *et al.* (2024), suggest that the use of bioidentical estrogens, which have a chemical structure closer to that of natural estrogen, may be an effective alternative for patients experiencing side effects with traditional synthetic estrogens. However, this approach still lacks further clinical studies to fully evaluate its long-term efficacy and safety.

Continued research in the area of hormone replacement is crucial to better understand the long-term effects and best practices for different patient groups. Research on hormone therapy has advanced significantly in recent years, with new studies focused on personalizing treatment based on biomarkers and genetic characteristics of patients (Kumar *et al.*, 2023). The latest evidence suggests that in the future, it will be possible to offer even more precise hormonal therapies, with fewer adverse effects and optimized clinical outcomes.

Although hormone replacement is a mainstay in the treatment of post-gonadectomy women, it is also important to consider therapeutic alternatives, especially in cases where hormone therapy is not indicated or desired. The use of non-hormonal therapies, such as selective estrogen receptor modulators (SERMs), has shown efficacy in some patients, especially those with contraindications to estrogen use (Smith *et al.*, 2023). However, these alternatives should be carefully evaluated and monitored due to their adverse effect profile and the need for individualized adaptation.

Finally, the decision about starting hormone replacement should be made together with the patient, considering the risks and benefits of the treatment. The role of healthcare professionals is to provide clear and detailed information about the options available, allowing the patient to make an informed decision. Individualization of treatment is key to ensuring that hormone replacement is a safe and effective therapy that contributes to patients' bone, cardiovascular, and psychological health over time.

FINAL CONSIDERATIONS

Post-gonadectomy hormone therapy in Morris Syndrome is essential for the overall health of patients. The proper use of estrogens contributes to the maintenance of bone, cardiovascular and psychological health.

The choice of estrogen type and clinical monitoring are essential to minimize adverse effects and optimize the quality of life of patients. Treatment adherence should be encouraged through multidisciplinary follow-up.

Future research should explore new therapeutic regimens and complementary interventions to ensure individualized, evidence-based care.

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