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PHARMACOLOGICAL AND SURGICAL APPROACHES TO THE MANAGEMENT OF ENDOMETRIOSIS

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Abstract: Endometriosis is a gynaecological disease characterized by the presence of endometrial tissue outside the uterus, causing chronic pain and infertility in many women. The treatment of endometriosis involves pharmacological approaches, such as the use of estroprogestins and GnRH agonists, and surgical interventions to excise the lesions. The choice of treatment depends on the severity of the symptoms, the location of the lesions and the patient's individual response. The management of endometriosis remains a challenge due to resistance to treatment, the variability of the lesions and post-treatment recurrences. This paper reviews the latest treatments, highlighting the advances and difficulties in managing the disease, with a focus on personalizing therapy to meet the needs of each patient.

Keywords: Endometriosis, Pharmacological treatment, Surgical excision, Personalized therapy, Pelvic pain, Infertility, Pathophysiology.

INTRODUCTION

Endometriosis is a complex gynecological condition that affects a significant proportion of women of reproductive age, with an estimated prevalence of between 6% and 10% of the female population. It is characterized by the presence of endometrial tissue outside the uterine cavity, usually in the peritoneum, which can also affect other organs. The etiology of the disease is not fully understood, but the retrograde menstruation theory is widely accepted, suggesting that endometrial cells flow back into the pelvic cavity during menstruation, settling in ectopic locations. However, in recent years, the genetic-epigenetic (GE) theory has gained prominence, proposing that endometriosis is triggered by a series of genetic and epigenetic alterations that allow pluripotent cells to differentiate into endometrial tissue outside the uterus. These alterations partly

explain the variability of the disease, such as the difference in responses to hormonal treatments and pain patterns between patients. The evolution of endometriotic lesions is also associated with environmental factors, including retrograde menstruation and the peritoneal microbiome, which suggests a complex interaction between genetics, epigenetics and the environment in the development of the disease. (AMRO et al., 2022)

The symptoms of endometriosis are varied, including chronic pelvic pain, dyspareunia, menorrhagia and, in many cases, infertility. Although laparoscopy is the standard method for diagnosis, imaging tests such as ultrasound and MRI play a key role in the pre-surgical assessment of lesions. Classifying the disease into minimal, mild, moderate and severe stages helps guide treatment, although the severity of the lesions does not always correlate with the intensity of the symptoms. In addition, recent studies highlight that the immune response plays a crucial role in the viability and growth of endometriotic tissue, with chronic inflammation contributing to prolonged pain and the formation of fibrosis around the lesions. (PAŠALIĆ; TAMB UWALA; HROMIĆ-JAHJEFENDIĆ, 2023) Recognizing these variabilities has enabled advances in therapeutic approaches, taking into account the specific characteristics of each patient, such as resistance to certain hormones or the presence of remote neuroinflammation, which alters the appropriate treatment.

The treatment of endometriosis is multifaceted, involving pharmacological and surgical options. Hormonal therapies, such as oral contraceptives, progestogens and GnRH analogues, are often used to control the growth of endometrial tissue and relieve symptoms. However, the effectiveness of these therapies can be variable, with some patients showing resistance to the hormones. The surgical approach, on the other hand, focuses on exci-

sing the endometriotic lesions, with laparoscopy being the technique of choice. In cases of cystic ovarian endometriosis and deep endometriosis, conservative excision is generally preferred, with removal of the lesions without the need for safety margins around the fibrous areas. In addition, superficial removal of cystic ovarian lesions is often sufficient to achieve symptom relief. A more detailed understanding of the pathophysiology of endometriosis, including the characteristics of the lesions and the associated risk factors, has allowed treatment to be personalized, promoting a more effective and less invasive approach. (KONINCKX et al., 2021)

The search for an early diagnosis, combined with more targeted treatments, represents a significant advance in the management of endometriosis, offering better prospects for disease control and quality of life for affected women. (PAŠALIĆ; TAMB UWALA; HROMIĆ-JAHJEFENDIĆ, 2023)

METHODOLOGY

The methodology adopted for the literature review aimed to synthesize the latest information on pharmacological and surgical approaches to the management of endometriosis. To do this, a search was carried out in the PubMed database, using the descriptors 'Endometriosis' and 'Treatment', in order to select relevant articles published in the last five years. The articles included were those that specifically addressed the treatment of endometriosis, considering both pharmacological and surgical approaches. Studies that were not available in the PubMed database or that did not meet the inclusion criteria, such as those that did not deal directly with therapeutic interventions, were excluded. In addition, duplicate articles or those with significant methodological flaws were disregarded. The selection was carried out carefully, with the aim of ensuring that the studies were cur-

rent, relevant and of high quality, ensuring the reproducibility and transparency of the process. Based on this analysis, the information extracted was organized in such a way as to provide an up-to-date overview of the different treatment options for endometriosis, highlighting the most recent advances and challenges.

RESULTS AND DISCUSSION

Endometriosis is a multifaceted clinical condition that requires a personalized therapeutic approach, given the variability of the lesions and the symptoms presented by patients. Pharmacological treatment remains a central option, with the widespread use of estroprogestins, progestins and GnRH agonists or antagonists, whose therapeutic effects are well documented. However, the effectiveness of these treatments is not uniform, with a satisfactory response in approximately 70% of patients, but minimal or non-existent relief in 10% to 20% of cases. This variability in response can be attributed to the heterogeneity of endometriotic lesions, which makes it difficult to predict the effectiveness of treatments and requires therapeutic adjustments over time. Periodic evaluation of the treatment using ultrasound every 6 months has been suggested to monitor the evolution of the lesions, since they can continue to grow even with continued use of the medication. (KONINCKX et al., 2021)

In addition, the pathophysiology of endometriosis, characterized by high estrogenic activity in the lesions, justifies the medical approach aimed at reducing circulating estrogen and progesterone levels, particularly in peritoneal lesions, where these hormones are present in significantly higher concentrations than in plasma. However, the effectiveness of this strategy continues to be debated, since some lesions can develop resistance to progesterone and show aromatase activity, which

makes treatment more complex. This resistance may be related to specific clonal characteristics of the lesions, which show distinct biochemical behaviors, making it difficult to choose a single, effective treatment for all patients. (AMRO et al., 2022; KONINCKX et al., 2021)

Surgically, excision of endometriosis lesions remains the preferred approach in many cases, with the aim of removing as much endometriotic tissue as possible with minimal damage to adjacent tissues. Surgical excision is especially recommended for deep lesions and in critical locations, such as the intestine and ureters, where lesions can cause significant complications, such as intestinal obstruction and ureteral stenosis. The strategy of conservative excision is discussed, based on the theory that fibrosis can be considered part of the body, which allows for a less invasive approach, with short resections and without the need for wide resections, as occurs in some more aggressive procedures. The use of techniques such as laser vaporization for superficial lesions and chemical destruction, such as alcoholization, for larger lesions, have been suggested as therapeutic options that minimize the risk of recurrence and post-operative adhesions, a frequent problem in more invasive interventions. (AMRO et al., 2022)

However, it is important to note that the surgical approach is not without its challenges. Recurrences are seen, especially in areas such as the vaginal dome, where wide excision is considered the best strategy to avoid new lesions. Additionally, the role of neural invasion in pelvic pain associated with endometriosis is still uncertain, and how this affects the surgical approach and pain resolution remains a field. (AMRO et al., 2022)

CONCLUSION

In short, the review carried out shows that the management of endometriosis requires an individualized therapeutic approach, given the complexity and variability of the clinical manifestations of the disease. Pharmacological treatments, which include the use of estroprogestins, progestins and GnRH agonists, have shown significant efficacy in a considerable proportion of patients, although resistance to these hormones and the heterogeneity of the lesions represent major challenges. At the same time, surgical interventions, especially lesion excision, remain essential, especially in cases of deep endometriosis and in critical locations, despite the risk of recurrence and the complications inherent in invasive procedures.

Faced with this scenario, personalizing treatment has emerged as a central element for therapeutic success, requiring the integration of clinical, imaging and, where possible, molecular data to guide the choice between pharmacological and surgical approaches. Improved diagnostic methods and continuous research into new therapeutic strategies are essential to optimize the management of the disease, minimizing complications and improving the quality of life of affected women.

Therefore, the treatment of endometriosis must be conceived in a dynamic and adaptive way, respecting the particularities of each patient and the challenges inherent in the evolution of the disease.

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