

ADVANCES IN THE MANAGEMENT OF ENDOMETRIOSIS: CURRENT DIAGNOSTIC AND THERAPEUTIC APPROACHES

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Abstract: This scientific article offers a comprehensive overview of endometriosis, covering diagnostic methods and available therapeutic options. The research methodology included a comprehensive search in three academic databases (Google Scholar, Scielo and PubMed) from 2004 to 2023, encompassing articles in English, Portuguese and Spanish. The search used relevant keywords and established inclusion criteria. The diagnosis of endometriosis involves an approach that takes into consideration, clinical evaluation, imaging tests, such as transvaginal ultrasound and magnetic resonance imaging, and analysis of the serum marker CA-125. Laparoscopy is usually necessary for a definitive diagnosis, although it is invasive. Endometriosis treatment is highly personalized, focusing on resolving pelvic pain and managing infertility when present. Therapeutic options include drug treatment, surgery and assisted reproduction treatments. The choice of treatment depends on several factors, such as the stage of the disease and other clinical factors. Drug treatment includes different hormonal approaches, but ovarian suppression alone is not recommended to improve fertility except in preparation for IVF. Surgical therapy ranges from less complex procedures to more extensive interventions, focusing on organ conservation. Conservative surgery is preferred as there is no direct correlation between the extent of the disease and the severity of symptoms. Lesion ablation and adhesiolysis can improve fertility, especially in mild to moderate cases. Therefore, it is concluded that the treatment of endometriosis requires a personalized approach, considering the symptoms, stage of the disease and the patient's reproductive goals, with the aim of providing pain relief and improving quality of life. Diagnosis and treatment must be carefully considered in each case.

Keywords: Endometriosis, pharmacology, diagnosis, therapy

METHODOLOGY

The methodology used in this scientific article involved a comprehensive search based on three renowned academic databases: Google Scholar, Scielo and PubMed. The research period was established from 2004 to 2023, covering recent publications related to endometriosis. Articles were included in English, Portuguese and Spanish, in order to guarantee a comprehensive analysis of the topic.

The search strategy was developed using relevant keywords, such as “endometriosis diagnosis,” “endometriosis treatment,” “endometriosis management,” “endometriosis therapy,” “endometriosis surgery,” and “endometriosis pharmacological treatment,” which were combined with Boolean operators “AND” and “OR” to refine the results.

Inclusion criteria were established that covered studies published within the research period, available in the languages mentioned and that addressed the diagnosis, treatment, drug therapy and surgery of endometriosis. Studies that were not directly related to the topic or were not available in full were excluded.

Relevant data was collected from the selected articles, including information on diagnostic methods, treatment options, pharmacological therapies and surgery. Factors such as efficacy, side effects and clinical recommendations were recorded.

The results of this review were organized in a clear and structured way, addressing aspects related to the diagnosis of endometriosis, therapeutic options, drug treatment and surgery, with the aim of providing a comprehensive and updated view of the knowledge available on the subject.

INTRODUCTION

Endometriosis is a benign, chronic and multifactorial gynecological disease. It is a comorbidity of functional endometrial tissue outside the uterine cavity and myometrium.

It affects women of reproductive age and it is known that at an early stage it is generally underdiagnosed, which is why it has been the subject of extensive investigation (Rosa et al., 2021, p. 135). Due to the great impact on women’s lives, both physical and psychological, it has become a public health problem. Several evidence-based theories were proposed throughout the 20th century to try to explain the etiology of Endometriosis. Progressively, new studies are being carried out with the aim of understanding the disease, as well as its diagnosis and treatment (Rosa et al., 2021, p. 135).

The investigation of Endometriosis begins with the patient’s anamnesis, with important points being personal history, family history, symptoms and subsequently the physical examination. If the patient is at high risk, they will undergo more detailed diagnostic procedures such as transvaginal Ultrasound, Magnetic Resonance Imaging, CA-125 and Laparoscopy (Rosa et al., 2021, p. 136). It is noteworthy that imaging exams are effective in detecting and staging ovarian endometriomas and deep lesions (PODGAEC, et al., 2020, p. 234). Furthermore, the time taken to make the diagnosis is long, which creates many frustrations in the patient’s life, mainly due to the progression of the disease (Rosa et al., 2021, p. 2).

As it is a chronic disease, it is important that women undergo follow-up care, especially during their reproductive years. Treatment aims to alleviate symptoms and improve the patient’s quality of life; it is not possible to cure the disease, only to control the clinical condition and control its progression (PODGAEC, et al., 2020, p. 234).

Progestins used continuously have been shown to be effective when related to pelvic pain caused by Endometriosis. The prescribed oral medications are norethindrone acetate, desogestrel and dienogest. The depot is medroxyprogesterone acetate and the long-lasting intrauterine device (IUD) releasing levonorgestrel, in addition to the etonogestrel implant.

Non-steroidal anti-inflammatory drugs are widely used to control primary dysmenorrhea, but there is no scientific evidence for their precise use in the disease, only for momentary pain relief in these patients. If clinical treatment is ineffective or there is a contraindication, minimally invasive surgical treatment via videolaparoscopic surgery must be chosen. In this context, the objective is the complete excision of all endometriosis foci. (PODGAEC, et al., 2020, p. 235).

DEVELOPMENT

DIAGNOSIS OF ENDOMETRIOSIS

Endometriosis is an estrogen-dependent disease that is defined by the presence of tissue that resembles the gland and/or endometrial stroma outside the uterine cavity, predominantly in the female pelvis (PODGAEC, et al., 2020, p. 233). The pathophysiology of the disease is still the subject of discussion and presents variables in its clinical and experimental evidence (PODGAEC, et al., 2020, p. 233). It is believed that several factors help in the spread of the disease, including: genetic, dietary, immunological and environmental (BARBOSA; OLIVEIRA, 2015, p.44). It is mainly characterized by chronic pelvic pain and infertility, and may be asymptomatic in 3 to 22% of patients. There are also other common symptoms such as dysmenorrhea, dyspareunia, dysuria and dyschezia. Its prevalence is 5 to 15% in women

of reproductive age and around 3% in postmenopausal women. Generally, chronic pelvic pain is the most prevalent symptom, in addition, psychological symptoms such as anxiety and depression and decreased quality of life are associated with the condition (MARQUI, 2014, p. 98). Endometriosis is classified as stage I (minimal), stage II (mild), stage III (moderate) or stage IV (severe), taking into consideration, the depth of the implants and types of adhesions in the ovarian tube, according to the American Society of Reproductive Medicine/ASRM (MARQUI, 2014, p.99). The investigation of Endometriosis begins with the patient's clinical history, a complete check of symptoms suggestive of the disease must be carried out. It is important to discuss personal and family history and also perform a physical examination. The gold standard diagnosis used for Endometriosis is laparoscopy (ROSA, et al., 2021, p. 136).

Videolaparoscopy is a minimally invasive technique performed using an endocamera that is inserted into the abdominal cavity through small holes, so it is possible to perform a biopsy of the lesion and send it for anatomopathological evaluation (MARQUI, 2014, p. 98). It is known that surgical diagnosis, in addition to having high potential, has disadvantages such as hemorrhages, infections, organ damage, adhesion formation and anesthetic complications. As well as high financial costs for the patient and the healthcare system. However, the definitive diagnosis is only made by laparoscopy (ROSA, et al., 2021, p. 136). However, it is only indicated for patients who had normal exams and failed clinical treatment, otherwise imaging exams are preferable as they are not invasive (PODGAEC, et al., 2020, p. 234). Transvaginal ultrasound and magnetic resonance imaging are routinely requested tests for the detection and staging of Endometriosis. Studies report that MRI is

superior to transvaginal ultrasound, as it has the limitation of identifying lesions in the upper abdominal region, as well as depending on an operator, however, MRI has greater difficulty in access due to its high cost (ROSA, et al., 2021, p. 136). It is also common to request laboratory tests, such as the serum biomarker CA-125, which has diagnostic potential for moderate to severe endometriosis (ROSA, et al., 2021, p. 136). However, there is no specific injury marker for the disease, which is an object of study for researchers seeking a non-invasive diagnostic method (NOGUEIRA, et al., 2018, p. 41).

THERAPIES FOR ENDOMETRIOSIS

The therapeutic approach to endometriosis is highly individualized, varying depending on the patient's main complaint, which often involves pelvic pain or fertility issues. The most prevalent therapeutic options at the moment include surgery, ovarian suppression therapy and a combination of these approaches. (NÁCUL, Andrea Prestes, 2010)

In situations where the patient's complaint is pelvic pain and minimal or mild endometriosis is suspected, it is possible to start empirical treatment with oral contraceptives, even before a definitive diagnosis, based on clinical evaluation. If the patient does not show improvement within a period of three months or if there is evidence of deep infiltrative endometriosis, therapy can be complemented with the use of gonadotropin-releasing hormone (GnRH) analogues, known as GnRHa, for the same period, followed by maintenance with oral contraceptives. (NÁCUL, Andrea Prestes, 2010)

However, if the patient has a recurrence of pain, imaging tests indicating the presence of an endometrioma larger than 3 cm in diameter or suspected intra-abdominal adhesions, laparoscopic surgery is recommended as the

next step in treatment, aiming to provide relief of symptoms. and improve the patient's quality of life. (Kennedy S, et al. 2005).

DRUG TREATMENT OF ENDOMETRIOSIS

In the context of treating pain associated with endometriosis, several pharmacological approaches have been extensively researched and applied. Among these approaches, estrogenic combinations, isolated progestogens and gonadotropin-releasing hormone (GnRH) analogues stand out. These therapeutic modalities primarily act by inhibiting the growth of endometriotic implants through mechanisms such as decidualization and endometrial atrophy, or by suppressing ovarian steroid hormones, resulting in the induction of a state of hypoestrogenism. (Davis L, et al. 2007)

Studies that investigated these hormonal therapies indicate that they all demonstrate similar effectiveness in reducing pain associated with endometriosis. However, it is imperative to highlight that these treatments present significant variations in terms of adverse effects and associated costs (Selak V, et al. 2007). It is crucial to note that all pharmacological therapies available for the management of pain due to endometriosis also have contraceptive properties. However, it is common to find patients facing both pain and infertility, especially in the more advanced stages of the disease, which makes the choice of these therapies challenging. There is no evidence to support the use of isolated ovarian suppression, through hormonal therapy, to improve fertility in patients with endometriosis, regardless of the stage of the disease, and this treatment also delays the possibility of pregnancy due to its contraceptive effect. Furthermore, pre- or post-operative treatments with medications that suppress ovarian function do not seem to

promote an improvement in fertility in these patients. (Yap C, et al. 2004)

The only situation in which ovarian suppression therapy is indicated in infertile patients with endometriosis is in preparation for in vitro fertilization (IVF). A recent Cochrane review demonstrated that the use of GnRH analogues for a period of three to six months before IVF significantly increased the chances of pregnancy by up to four times. (NÁCUL, Andrea Prestes, 2010) However, it is important to highlight that these results are based on a single clinical trial with a small sample size and methodological issues. Therefore, the decision to adopt prior therapy with GnRH analogues must be individualized, taking into consideration, the presence of factors that may influence the patient's response to ovarian stimulation, such as compromised ovarian reserve. (Davis L, et al. 2007)

ASSISTED REPRODUCTION TREATMENTS IN THE MANAGEMENT OF INFERTILITY IN PATIENTS WITH ENDOMETRIOSIS

The management of infertility in patients affected by endometriosis requires the consideration of assisted reproduction treatments, notably intrauterine insemination and in vitro fertilization. The decision regarding the appropriate therapeutic strategy is based on the careful analysis of several parameters, such as the stage of endometriosis, the integrity of the Fallopian tubes, the patient's age, the duration of infertility and the coexistence of aggravating factors. (NÁCUL, Andrea Prestes, 2010)

Intrauterine insemination with ovulation induction emerges as an effective approach in scenarios of minimal or mild endometriosis, provided that pelvic anatomical integrity is preserved, at least one fallopian tube remains functional, and sperm parameters meet

stringent criteria, including higher sperm concentration. at 5 million/mL. This treatment modality can be administered for a maximum period of six cycles. Patients over the age of 35 can directly opt for in vitro fertilization (IVF). (Benaglia L, et al. 2010)

IVF is the appropriate therapeutic alternative in cases of endometriosis classified as grade 3 or 4, in the presence of tubal involvement, associated male factors or failure in previous therapeutic attempts. It is important to highlight that the current literature does not show a substantial correlation between the number of IVF cycles and the recurrence of endometriosis. (Benaglia L, et al. 2010)

SURGICAL TREATMENT

The surgical approach to endometriosis encompasses a wide range of procedures, from low-complexity interventions, such as cauterization of superficial lesions and release of adhesions, to more complex surgeries involving organs such as ovaries, cul-de-sac, intestine, bladder and ureters., often requiring a multidisciplinary team. (PODGAEC et al., 2020)

For many years, surgical treatment of endometriosis was based on the premise of radical removal of lesions, following oncological principles. This approach is still applied in cases of intestinal or ureteral stenosis, as well as in the presence of ovarian masses with uncertain characteristics. However, we currently understand that there is no direct correlation between the extent of the disease, the severity of symptoms, reproductive prognosis and long-term pain recurrence. Additionally, many patients face not only pain but also infertility, making it necessary to adopt a conservative surgical approach. Based on this understanding, some experts recommend surgery only for those patients who do not respond to drug

treatment or for those who seek to become pregnant spontaneously. (ANDREA DE ALBUQUERQUE et al., [2006])

It is important to note that there are few published randomized clinical trials that evaluate the results of surgical treatment of symptomatic endometriosis. A review by Vercellini reported symptomatic improvement after conservative treatment in a range of 60% to 80%, with variable rates of symptom recurrence and reoperation, ranging from 12% to 58% between studies. (Vercellini P, et al. 2009)

With regard to patients with infertility, lesion ablation and adhesiolysis appear to provide improvements in fertility in cases of mild to moderate endometriosis. However, for more severe cases, there is a gap in evidence from randomized clinical trials or meta-analyses to indicate whether lesion resection increases pregnancy rates. (PODGAEC et al., 2020)

CONCLUSION

In short, the diagnosis of endometriosis involves a comprehensive approach, considering clinical evaluation, imaging tests, such as transvaginal ultrasound and magnetic resonance imaging, and, in suspected cases, analysis of the CA-125 serum marker. Definitive diagnosis is usually obtained through laparoscopy, although it is an invasive procedure with disadvantages. (MARQUI,

2014, p. 99).

Therapy for endometriosis is highly individualized, prioritizing resolution of pelvic pain and management of infertility, if present. Therapeutic options include drug treatment, surgery and, in cases of infertility, assisted reproduction treatments such as intrauterine insemination and in vitro fertilization. The choice of treatment depends on several factors, such as the stage of the disease, anatomical integrity and other clinical factors. (NÁCUL, Andrea Prestes, 2010)

In drug treatment, different hormonal approaches have been shown to be effective in reducing pain, although with variations in side effects and associated costs. Ovarian suppression alone is not recommended to improve fertility except in preparation for IVF. (Davis L, et al. 2007)

Surgical therapy ranges from less complex procedures to more extensive interventions, with a focus on organ conservation. Currently, conservative surgery is preferred as there is no direct correlation between the extent of the disease and the severity of symptoms. Lesion ablation and adhesiolysis can be effective in improving fertility, especially in mild to moderate cases. (PODGAEC et al., 2020)

Therefore, the treatment of endometriosis requires a personalized approach, considering the patient's symptoms, stage of the disease and reproductive goals, aiming to provide pain relief and improve quality of life.

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