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Medical treatment and other non-surgical therapeutic tools in symptomatic endometriosis

Tratamiento médico y otras herramientas terapéuticas no quirúrgicas en endometriosis sintomática

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ABSTRACT
Endometriosis is a disease that affects millions of women worldwide and significantly impacts their quality of life, including professional and psychological aspects. This article addresses the comprehensive management of symptomatic endometriosis, focusing on non-surgical therapeutic alternatives. The treatment of symptomatic endometriosis requires a personalized and multidisciplinary approach, combining medical therapies (both hormonal and non-hormonal), pelvic floor rehabilitation, and psychological support. Long-term medical therapy, including maintenance treatment after surgery, is often recommended to control pain and reduce recurrence. Throughout the process, the patient's needs and active participation in treatment decisions should be prioritized.
Keywords: endometriosis / pelvic pain / dysmenorrhoea / medical treatment.

RESUMEN
La Endometriosis es una enfermedad que afecta a millones de mujeres globalmente y que impacta significativamente su calidad de vida, incluyendo aspectos laborales y psicológicos. En este artículo se aborda el manejo integral de la endometriosis sintomática en sus alternativas no quirúrgicas. El tratamiento de la endometriosis sintomática requiere un enfoque personalizado y multidisciplinario, combinando terapias médicas (hormonales y no hormonales), rehabilitación pelviperineal y apoyo psicológico. La combinación de terapia médica a largo plazo, incluso post-cirugía, es a menudo recomendada para controlar el dolor y reducir la recurrencia, siempre priorizando las necesidades y la participación activa de la paciente en las decisiones de su tratamiento.
Palabras clave: endometriosis / dolor pélvico / dismenorrea / tratamiento médico.

Introduction

According to the WHO, endometriosis affects 10% of women of reproductive age, which means that approximately 190 million women worldwide suffer from this disease. Its most common symptoms are infertility and cyclical or continuous pain, which may or may not be associated with dyspareunia, dyschezia, urinary symptoms, and sometimes significant anxiety and depression[1].

According to a recent study of Scandinavian women, endometriosis is also associated with work problems or absenteeism, sick days, or disability, which is in line with studies conducted in other countries[2,3,4].

This chapter will mainly describe medical treatments related to pain, as it is estimated that 40-70% of women with chronic pelvic pain and approximately 50% of women with secondary dysmenorrhea suffer from endometriosis[5,6]. This review will include non-hormonal medical treatments, including non-steroidal anti-inflammatory drugs and neuromodulators, hormonal treatments, including GnRH agonists and antagonists, as well as kinesiological and psychological support for these patients.

Non-hormonal pain management in endometriosis

Pain management in patients with endometriosis is complex and requires careful assessment to identify the type of pain present. Differentiating between types of pain is essential for establishing appropriate treatment. In this context, pain in endometriosis can be classified into three types according to the definition of the International Association for the Study of Pain (IASP):

1. Nociceptive pain: Arises from inflammatory mechanisms related to the presence of tissue lesions. In endometriosis, this pain originates from inflammation of ectopic endometrial lesions, activating peripheral nociceptors[7].

2. Neuropathic pain: Results from damage or dysfunction of the somatosensory nervous system and may coexist with nociceptive pain in patients with endometriosis, especially when nerve structures are compromised[8].

3. Nociplastic pain: This is caused by alterations in nociception, without the presence of tissue damage or known injury to the nervous system. In some cases of endometriosis, there may be a nociplastic component that contributes to chronic pain, characterized by central and peripheral sensitization[9].

The coexistence of these types of pain in endometriosis requires a multidisciplinary and personalized approach, with therapies targeting each component.

Management of Nociceptive Pain

Nociceptive pain in endometriosis is mainly due to inflammation caused by endometrial lesions. The following treatments are effective:

1. Nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen:

    - Mechanism of action: NSAIDs inhibit cyclooxygenase (COX), reducing the production of prostaglandins, key mediators of inflammation and pain. Paracetamol acts mainly centrally, inhibiting prostaglandin synthesis in the central nervous system.
    - Dosage:
        - Ibuprofen: 400-600 mg every 8 hours, up to a maximum of 2400 mg/day. Studies demonstrate its effectiveness in reducing inflammatory pain[10].
        - Naproxen: 250-500 mg every 12 hours. It is preferred due to its longer half-life and lower frequency of administration.
        - Paracetamol: 500-1000 mg every 8-12 hours, maximum 4 g/day. It is useful in patients with contraindications for NSAIDs.
    - Combination: The combination of NSAIDs and paracetamol has been shown to be more effective in reducing pain than monotherapy[10].

2. Opioids:

    - Mechanism of action: They act on opioid receptors in the central nervous system, modulating pain perception.
    - Dosage and evidence:
        - Tramadol: 50-100 mg every 6-8 hours, not exceeding 400 mg/day. It is a weak opioid with dual activity (opioid and serotonergic).
        - Codeine: 15-60 mg every 4-6 hours, maximum 120 mg/day. Requires conversion to morphine for analgesic activity.
        - Potent opioids (morphine, oxycodone): Reserved for severe and refractory cases, under strict supervision.
    - Considerations: Its use should be limited due to the risk of dependence, tolerance, and adverse effects such as constipation and sedation[11].

Management of Neuropathic Pain

Neuropathic pain in endometriosis may result from damage to nerve structures or central sensitization.

1. Anticonvulsants: These have been shown to be effective in managing neuropathic pain associated with endometriosis[12].

   - Mechanism of action: They modulate pain transmission by reducing neuronal excitability and the release of excitatory neurotransmitters.

   - Dosage:

     - Pregabalin:

       - Initial dose: 75 mg twice daily.

       - Increase gradually to 150 mg twice daily, depending on tolerance and response.

       - Maximum dose: 300 mg/day.

     - Gabapentin:

       - Initial dose: 300 mg daily, in one or two doses.

       - Gradual increase: up to 900-1800 mg/day in 3-4 doses, depending on tolerance.

2. Dual antidepressants (SNRI): Effective in managing chronic neuropathic pain[13].

   - Mechanism of action: They inhibit the reuptake of serotonin and norepinephrine, modulating pain transmission at the central level.

   - Dosage:

     - Duloxetine: Usual dose: 30-60 mg once daily. Maximum: 60 mg/day.

     - Venlafaxine: Initial dose: 37.5-75 mg once daily. Adjustments: up to 225 mg/day in refractory cases.

3. Tricyclic antidepressants (TCAs): Useful in patients with neuropathic pain and associated sleep disorders[13].

   - Mechanism of action: They block the reuptake of serotonin and norepinephrine, in addition to having antihistamine and anticholinergic effects.

   - Dosage: Amitriptyline: Initial dose: 10-25 mg at night. Maintenance dose: 25-75 mg/day, adjusting according to tolerance and response.

Management of Nociplastic Pain

Nociplastic pain requires a multidisciplinary approach that includes pharmacological and non-pharmacological therapy.

1. Adjuvants:

   - Omega-3 fatty acids (EPA and DHA): Studies suggest that they reduce inflammation and improve chronic pain symptoms[14].

     - Mechanism of action: They modulate inflammation by inhibiting the production of proinflammatory cytokines and promoting the synthesis of anti-inflammatory mediators.

     - Dosage: 1-3 grams per day.

   - Magnesium citrate: Effective in reducing chronic pain and improving quality of life[15].

     - Mechanism of action: Regulates neuronal excitability and reduces central sensitization.

     - Dosage: 200-400 mg per day.

2. Non-pharmacological therapies:

   - Physical therapy: Relaxation and muscle strengthening exercises.

   - Cognitive behavioral therapy (CBT): Helps manage the psychological impact of chronic pain.

   - Acupuncture: Can modulate pain perception and reduce central sensitization.

Other therapies for treatment-refractory pain:

Ketamine infusions:

Ketamine is used in certain cases of neuropathic pain due to its analgesic and nervous system modulating properties. Its mechanism of action, as an antagonist of NMDA (N-methyl-D-aspar-

tate) receptors, is involved in pain transmission and central sensitization. Studies show an effective reduction in pain and improvement in quality of life, but the effects may be temporary and will vary between individuals[16,17]. Ketamine infusion is a specialized treatment, ideally administered in a controlled clinical setting, and should be considered as part of a multidisciplinary approach to the management of neuropathic pain.

Indications for Neuropathic Pain

- Refractory chronic pain: Especially useful in cases where other treatments have been ineffective[16].
- Complex regional pain syndromes (CRPS)[18].
- Pain associated with nerve damage or of central origin[17].

Infusion Protocol:

- Dosage: Varies according to protocol, generally starting with low doses (0.1-0.5 mg/kg/h) [19].
- Duration: May vary from a few hours to several sessions spread over days or weeks.
- Route of administration: Intravenous under monitored supervision.

Side Effects:

- Immediate: Nausea, dizziness, sedation, perceptual disturbances.
- Long-term: Renal or bladder complications with prolonged use.

Contraindications:

- Patients with a history of severe psychiatric illness or uncontrolled hypertension.

Lidocaine infusions:

Lidocaine infusions are another option for managing neuropathic pain and some types of chronic pain. Their mechanism of action is based on blocking sodium channels in neuronal membranes, reducing the excitability of nerve fibers.

Indications for Neuropathic Pain:

- Chronic neuropathic pain: Used when other treatments have not been effective[20].
- Persistent postoperative pain.
- Complex regional pain syndrome (CRPS)[21].

Infusion Protocol:

- Dose: Generally starts at 1 mg/kg/hour for 5 hours.
- Duration: The protocol depends on the patient and the type of pain.
- Route of administration: Intravenous in a controlled clinical setting.

Side Effects:

- Immediate: Dizziness, nausea, tinnitus, drowsiness.
- Toxicity: At high levels, it can cause more serious effects such as seizures or heart block[22].

Considerations:

- Monitoring: Necessary during infusion to watch for signs of toxicity.
- Contraindications: Patients with allergies to local anesthetics or severe heart problems.

Interventional pain therapies:

Interventional management of chronic pain in endometriosis often includes nerve and sympathetic block techniques. These interventions are aimed at relieving localized and visceral pain associated with this condition. The most commonly used techniques, according to the type of pain, are detailed below:

1. Pelvic and Abdominal Pain

   Superior hypogastric plexus block

   Effective for relieving pain in gynecological cancer and some non-malignant conditions[23].

- Indications: Visceral pain in the pelvis, particularly related to the uterus and bladder.
- Technique: A local anesthetic is injected into the anterior region of L5-S1 under imaging guidance.

Impar Ganglion Block

Significant relief of chronic pelvic pain and complex regional pain syndrome[24].

- Indications: Pelvic and perineal visceral pain.
- Technique: Injections into the presacral region, between the sacrum and coccyx.

2. Perineal pain

Pudendal nerve block:

Used successfully in pudendal neuralgia and chronic perineal pain[25].

- Indications: Vulvar and perineal pain.
- Technique: Injection into Alcock's canal under ultrasound guidance.

These blocks, performed in a clinical setting controlled by specialists, can provide significant relief and improve the quality of life for patients with chronic pain associated with endometriosis.

Table 1. Summary table of medications for pain management in endometriosis according to type of pain.

Type of pain	Medication	Mechanism of Action	Dosage	Daily Maximum	Considerations
Nociceptive	Ibuprofen	Inhibits COX, reducing inflammatory prostaglandins.	400-600 mg every 8 hours.	2400 mg/day	First line. Effective for inflammatory pain.
	Naproxen	Inhibits COX, with prolonged half-life.	250-500 mg every 12 hours..	1000 mg/day	Preferred due to lower frequency of administration.
	Acetaminophen	Inhibits prostaglandin synthesis in the CNS.	500-1000 mg every 8-12 hours.	4000 mg/day	Useful in patients with contraindications for NSAIDs.
	Tramadol	Acts on opioid receptors and modulates serotonin.	50-100 mg every 6-8 hours.	400 mg/day	Weak opioid. Risk of dependence.
	Codeine	Converts to morphine for its analgesic activity.	15-60 mg every 4-6 hours.	120 mg/day	Risk of constipation and sedation.
	Morphine	Acts on opioid receptors in the CNS.	Individualized dosage according to need.	As prescribed	Reserved for severe and refractory cases.
Neuropathic	Pregabalin	Modulates voltage-dependent calcium channels, reducing neuronal excitability.	Initial: 75 mg twice daily. Adjust up to 150 mg twice daily.	300 mg/day	Effective in neuropathic pain.
	Gabapentin	Similar to pregabalin, modulates pain transmission.	Initial: 300 mg daily. Adjust up to 900-1800 mg/day in 3-4 doses.	1800 mg/day	Requires gradual titration.
	Duloxetine	Inhibits serotonin and norepinephrine reuptake.	30-60 mg once daily.	60 mg/day	Useful in chronic neuropathic pain.
	Venlafaxine	Inhibits serotonin and norepinephrine reuptake.	Initial: 37.5-75 mg once daily. Adjust up to 225 mg/day.	225 mg/day	Effective in refractory cases.
	Amitriptyline	Blocks serotonin and norepinephrine reuptake.	Initial: 10-25 mg at night. Adjust up to 25-75 mg/day.	75 mg/day	Useful in patients with associated sleep disorders.
Nociplastic	Omega-3 fatty acids	They modulate inflammation and reduce pro-inflammatory cytokines.	1-3 grams per day.	3 grams/day	Nutritional supplement.
	Magnesium citrate	They regulate neuronal excitability and reduce central sensitization.	200-400 mg per day.	400 mg/day	Effective for chronic pain.

Non-hormonal pain management in endometriosis requires a personalized approach that considers the different types of pain present. The combination of pharmacological and non-pharmacological therapies, together with a multidisciplinary approach, offers the best opportunity to improve patients' quality of life.

3. Hormonal treatment

A common denominator of all hormonal drugs is the cessation of cyclic menstruation, either by suppressing ovarian estrogen secretion or by inducing a state of pseudopregnancy.

These drugs include combined oral contraceptives (COCs), progestins, gonadotropin-releasing hormone (GnRH) analogues, long-acting reversible contraceptives (LARCs), danazol, and aromatase inhibitors.

The effect of hormone therapy is to induce remission of the disease, but the reappearance of symptoms is to be expected when the drugs are discontinued for any reason. This is because the drugs control, but do not eliminate, the endometriotic foci[26].

It has been reported that, in addition to their effect on pain, these types of hormone therapies can also achieve a significant reduction in the size of ovarian endometriomas[27].

The drugs available for the medical hormonal treatment of pain caused by endometriosis include:

a. Combined oral contraceptives (COCs).

b. Progestins.

c. Long-acting systems.

d. GnRH analogues.

e. Others: Danazol and aromatase inhibitors.

a. Combined oral contraceptives (COCs)

Jensen et al., based on the results of a systematic review of the effects of COCs in women with symptomatic endometriosis, concluded that combined hormonal contraception or progestin-only contraception are affordable and effective treatment options for women with endometriosis. These methods reduce menstrual and non-menstrual pain and improve quality of life[28].

Table 2. Nonsteroidal anti-inflammatory drugs (NSAIDs) used in endometriosis.

Drug	Dosage
Paracetamol	500 mg to 1000 mg every 8 hours.
Diclofenac	50–75 mg every 12 hours.
Ibuprofen	Initial dose 800 mg followed by 400 to 800 mg every 8 hours.
Naproxen Sodium	Initial dose 440–550 mg followed by 220–550 mg every 12 hours.
Mefenamic Acid	500 mg followed by 250 mg every 6 hours.
Celecoxib	400 mg, then 200 mg every 12 hours.

Continuous use of COCs can also cause amenorrhea and, through this effect, further improve outcomes compared to cyclic use[27].

Grandi et al. confirmed that COCs are effective in relieving menstrual and pelvic pain associated with endometriosis, thereby improving patients' quality of life (QoL)[29].

On the other hand, Muzii et al. found that COCs used continuously were more effective in reducing the recurrence rates of postoperative dysmenorrhea than COCs used cyclically (risk ratio (RR), 0.24; 95% CI, 0.06–0.91). The differences between groups observed for dyspareunia and non-menstrual pain recurrence rates were not statistically significant[30].

b. Progestins

According to the results of the systematic review by Mitchell et al. (2022), progestins significantly improved the pain symptoms associated with endometriosis during 6-12 months of treatment, with no substantial differences between the different types[31].

The median discontinuation rate due to side effects was 0.3% (range, 0-37%), with only mild events reported.

These findings are consistent with those published by Canis and Guo (2023), who state that progestins may lead to poor tole-

Table 3. Comparison of oral GnRH antagonists.

Feature	Elagolix	Relugolix	Linzagolix
Approval	FDA (2018) – USA	Approved in Japan and Europe (Gedeon Richter).	EMA (2022), approved in Europe.
Trade name	Orilissa.	Relumina (Japan), Ryeqo (combined in Europe).	Yselty (Europe).
Main indication	Endometriosis pain.	Endometriosis (combined with estrogen and progestin).	Moderate-severe endometriosis.
Dosage	150 mg once daily (moderate) or 200 mg twice daily (severe).	40 mg once daily + hormone add-back.	75 mg (without add-back) or 200 mg (with add-back).
Onset of action	Rapid (days).	Rapid (days).	Rapid (days).
Estradiol suppression	Partial to complete (dose-dependent).	Complete (with standard doses).	Adjustable: partial (75 mg) or complete (200 mg).
Mandatory add-back therapy	Only with 200 mg twice daily (long duration).	Yes, as combination therapy.	Only with 200 mg doses.
Common side effects	Hot flashes, insomnia, decreased libido.	Hot flashes, headache, menstrual irregularity.	Hot flashes, headache, bone loss (high dose).
Effects on bone density	Decrease at 6 months (high dose).	Requires add-back to prevent bone loss.	Less with 75 mg; more with 200 mg.
Maximum recommended duration	6 months (high dose); 24 months (low).	Long duration possible with add-back.	≥24 months in studies.
Distinctive advantage	First approved, good dose flexibility.	Combined with COCs, good bone tolerance.	Allows treatment without add-back in mild cases.

rance and lower adherence to therapy due to an increased risk of depression and significant weight gain[32].

Most other studies related to progestins published in recent years have focused primarily on dienogest, but are limited to small retrospective and prospective studies.

In two studies, patients were assigned to treatment with dienogest 2 mg/day for 36 weeks (n=17) or 52 weeks (n=135) (Petraglia, et al., 2012, Strowitzki, et al., 2010). The study reported an improvement in pain for both the group previously treated with dienogest and the group previously treated with placebo (from 40.73 ± 21.14 to 13.49 ± 14.14 mm versus 27.89 ± 20.24 to 9.72 ± 7.44 mm, respectively). Adverse effects were reported in 27 of 168 women, including breast discomfort (n=7; 4.2%), nausea (n=5; 3.0%), and irritability (n=4; 2.4%)[33,34].

In another long-term study, the use of dienogest (2 mg/day) for 52 weeks was evaluated (Momoeda, et al., 2009). A reduction in the Visual Analog Scale (VAS) score for pelvic pain was observed after 24 and 52 weeks of treatment (-22.5 ± 32.1 and -28.4 ± 29.9 mm, respectively). All patients experienced some side effects, such as vaginal bleeding (71.9%), headache (18.5%), constipation (10.4%), nausea (9.6%), and hot flashes (8.9%). The percentage of patients with amenorrhea was 7.4% at 5 to 8 weeks and 40.5% at 49-52 weeks of treatment[35].

c. Long-acting systems

Several studies have shown that the LNG-52mg IUD has a local action that significantly reduces cyclic and non-cyclic pelvic pain at 6 months, with rates comparable to GnRH analogues and higher than combined hormonal contraceptives.

Postoperative use was associated with a lower recurrence rate of dysmenorrhea, especially in people with deep endometriosis or associated with adenomyosis, as well as a better quality of life compared to expectant management, although trials have shown a limited effect in patients with deep dyspareunia[36,37].

A recent RCT randomized 103 women with chronic pelvic pain associated with endometriosis and/or dysmenorrhea to a subdermal etonogestrel (ENG) implant or a 52 mg levonorgestrel-releasing intrauterine system (Margatho, et al., 2020). The study reported that both the ENG implant and the LNG-IUS significantly reduced pain related to endometriosis, dysmenorrhea, and chronic pelvic pain.

However, the study reported a high discontinuation rate and loss to follow-up at 24 months in both arms: 65% for the ENG implant and 63% for the 52 mg LNG-IUS (38).

d. GnRH analogues

GnRH analogues are divided into agonists and antagonists. Agonists initially induce the release of FSH and LH, then block E2 secretion for prolonged periods. When using depot injections, the effect may be slow to wear off.

Several studies have shown that GnRH agonists are more effective than combined hormonal contraceptives in treating pelvic pain associated with endometriosis and are similar in efficacy to the 52 mg LNG IUD and implants[26,35,39,40].

GnRH antagonists cause rapid blockade without gonadotropin release and a rapid drop in estradiol levels. These types of drugs have been developed for oral use, which allows for a more comfortable effect that is both rapid and reversible. Several studies have shown a 46% to 60% reduction in pelvic pain within 6 months.

One of the major concerns with this group of drugs is the loss of bone mineral density due to the hypoestrogenism associated with this type of therapy[35,40,41]. For this reason, replacement therapy with estrogen and progesterone ("add-back") is recommended. The administration of GnRH analogues, combined with "add-back" therapies from the outset, does not reduce the efficacy of the treatment.

One study showed that patients who used combined GnRH analogue and estrogen and progesterone (E+P) therapy from the outset had similar bone mineral density to the placebo group at 6 and 12 months of treatment. A randomized controlled clinical trial showed that GnRH analog administration without E+P replacement therapy for more than 6 months is associated with significant bone loss, without reaching osteoporosis. Delayed administration of estrogen and progesterone is associated with bone mass recovery after 6 months of replacement therapy[42].

Two clinical studies, called SPIRIT 1 and 2, investigated the efficacy and safety of a new oral hormone therapy option consisting of the combination of the GnRH antagonist relugolix, plus estradiol and norethisterone acetate (relugolix 40 mg, estradiol 1 mg, and norethisterone acetate 0.5 mg) for the treatment of pain associated with endometriosis in women[43].

These double-blind, placebo-controlled trials demonstrated that this therapy significantly improved menstrual and non-menstrual pelvic pain, reduced the use of analgesics and opioids, and improved quality of life compared to placebo.

The addition of estradiol and norethisterone acetate to relugolix was intended to maintain estradiol concentrations within a therapeutic range similar to that of the early follicular phase of the menstrual cycle. This was done to minimize vasomotor symptoms and bone mineral density loss seen with GnRH antagonists monotherapy, which profoundly suppress estradiol levels.

Adverse effects were generally similar across treatment groups, and bone mineral density loss was minimal with combination therapy.

Finally, GnRH analogues are often recommended as third-line therapy in individuals who do not respond to oral hormone treatment (combined or progestins alone) or extended-release systems[26,35,40,44].

e. Others

Danazol

This is a synthetic derivative of etisterone with androgenic, antiestrogenic, and antigonadotropic effects. It suppresses the production of gonadotropins (LH and FSH),

leading to hypoestrogenemia and anovulation, causing atrophy of endometriotic implants.

Danazol can cause severe or bothersome side effects, especially with prolonged treatment.

Among the most important are:

- Weight gain.
- Acne, oily skin.
- Hirsutism, deep voice.
- Changes in lipid profile (dyslipidemia).
- Breast atrophy.
- Liver disorders.
- Amenorrhea.

These effects, especially the virilizing ones, limit its use in young women and in prolonged treatments. That is why the current role of danazol in endometriosis is marginal. It is reserved for very select and refractory cases, due to its significant adverse effects[45,46].

Aromatase inhibitors

In women with endometriosis-related pain that is refractory to other medical or surgical treatment, there is some evidence supporting the prescription of aromatase inhibitors, as they reduce endometriosis-related pain. Aromatase inhibitors can be prescribed in combination with oral contraceptives, progestogens, GnRH agonists, or GnRH antagonists.

The evidence consists of a 2011 systematic review (Ferrero, et al., 2011) that includes mostly non-randomized controlled studies and case reports in women with rectovaginal endometriosis or women who are refractory to previous surgical and medical treatment, and two more recent studies. Evidence on the long-term effects of aromatase inhibitors is lacking.

Due to severe side effects (vaginal dryness, hot flashes, decreased bone mineral density), aromatase inhibitors should only be prescribed to women after all other medical or surgical treatment options have been exhausted[47].

Medical treatment as a pre- and post-operative adjunct

Preoperative hormonal medical treatment has been analyzed by the 2014 and 2022 ESHRE guidelines, with no clear differences in pelvic pain at 12 months or after surgery between patients who used and those who did not use this treatment[26,48].

The same applies to dysmenorrhea, dyspareunia, and recurrence of the disease. Therefore, the updated recommendation is not to prescribe preoperative hormonal medical treatment in order to improve the immediate outcome of surgery to treat pain due to endometriosis, although it can obviously be used while awaiting surgery.

With regard to postoperative hormonal medical treatment, and according to an extensive publication by Chen et al., considering only randomized studies and a large number of patients (3,338 patients), they show very moderate evidence in favor of the benefit of hormonal treatment up to 12 months post-surgery in order to improve the effect on pain when used alone to optimize the results of surgical therapy[49].

There is another randomized study, but with only a small number of patients, which shows a positive effect on dyspareunia and pelvic pain when a levonorgestrel intrauterine device is used post-surgery (hormonal method not included in the meta-analysis by Chen et al.)[36].

However, the ESHRE Guidelines recommend that post-operative hormonal treatment may be offered to improve the immediate results of surgery for endometriosis pain, provided that there is no desire to become pregnant immediately after the procedure[26].

Considerations and risks of long-term hormone therapy

Unlike surgery, the specific complications of long-term hormone therapy (>1 year), with the possible exception of COCs, have not been fully delineated.

There is concern about the possibility of malignant transformation of ovarian endometriotic lesions with long-term hormone therapy, although the risk is small and has not been thoroughly evaluated[46]. A notable exception is COCs, whose use for >10 years has been associated with an 80% reduction in the risk of ovarian cancer in women with endometriosis.

Other potential drawbacks of long-term hormone therapy include bone loss (especially with dienogest and GnRH agonists), a possible increased risk of depression with prolonged use of dienogest and combined oral contraceptives[50,51], weight gain associated with progestins alone, and the risk of venous thromboembolism with dienogest and GnRH antagonists.

Notwithstanding the above, hormonal medical treatment is a valid option for managing pain associated with endometriosis. The choice of treatment must be individualized and carefully consider the benefits, risks, and preferences of each patient.

It has been reported that three-quarters of women with superficial peritoneal and ovarian endometriosis and two-thirds of those with deep lesions are satisfied with their hormonal medical treatment[52,53,54], including patients with non-subocclusive colorectal disease[55,56].

When considering the use of hormonal treatments for endometriosis, the quality of information provided to patients about likely side effects and how to deal with them is crucial to ensuring optimal acceptability and, therefore, the effectiveness of therapy. In a study conducted via social media among more than 3,000 patients with endometriosis, potential side effects affecting mental health were the most important reason for rejecting hormonal therapies. At the same time, a considerable proportion of women reported having limited knowledge about these medications and indicated that social media was their most useful source of information[57].

Pelvic rehabilitation in endometriosis

Pelvic rehabilitation in the context of endometriosis focuses on treating pelvic floor dysfunction, managing associated pain, and improving the quality of life of people affected by this condition. A significant proportion of women with pelvic symptoms have been diagnosed with endometriosis, which, as already noted, is a chronic inflammatory disease that has a considerable impact on daily activities[6].

Despite growing global recognition of this condition, there remains a notable lack of studies that rigorously evaluate the effectiveness of pelvic floor rehabilitation interventions in this population. This lack of evidence limits the ability to establish with certainty the effectiveness of the various therapeutic strategies available[26].

In the field of rehabilitation, treatment is mainly focused on pelvic floor dysfunctions related to organs located inside and outside the pelvic cavity, such as the bladder, uterus, vagina, intestine, and musculoskeletal system. Techniques and instruments commonly used in pelvic floor rehabilitation include: pressure or electromyographic biofeedback, pelvic floor muscle training (PFMT), posterior tibial nerve neuromodulation (PTNM), transcutaneous electrical nerve stimulation (TENS), manual therapy and myofascial release techniques, and the use of physical agents such as moist compresses[58].

Electromyographic biofeedback

Electromyographic (EMG) biofeedback is a muscle retraining technique that allows the creation of new feedback systems by converting myoelectric signals generated by muscle activity into visual or auditory stimuli. This method uses surface electrodes to record variations in skeletal muscle activity, which are then transmitted to the patient in the form of perceptible signals, commonly visual or auditory. EMG biofeedback can be used both to enhance activation in weakened muscles and to promote tone inhibition in spastic muscles[59,60].

Pelvic floor muscle training

In 1947, Kegel defined pelvic floor muscle training (PFMT) as the voluntary contraction of the pelvic floor muscles (PFMs). Later, in 2004, Kari Bø proposed four key principles for training these muscles: 1- voluntary contraction of the PPM before and during increased intra-abdominal pressure (IAP) (e.g., during coughing), a technique known as “Knack” or perineal block; 2- functional trai-

ning, which involves the systematic application of perineal blocking in activities of daily living; 3- strength training of the PFM through structured programs over time; and 4- indirect training of the PFM through abdominal muscle exercises (transverse abdominis)[61].

The available evidence supports the existence of two distinct therapeutic approaches: on the one hand, the immediate application of perineal blockage as a preventive strategy to avoid urinary leakage induced by sudden increases in intra-abdominal pressure (IAP) and, on the other hand, the progressive strengthening of the PFM as a long-term intervention to improve their functionality and resistance[61].

With the aim of ensuring adequate progression in pelvic floor muscle (PFM) training, the methodological concept of the 5 Fs has been introduced: Find (Encontrar), Feel (Sentir), Force (Fuerza), Follow Through (Continuar hacia la funcionalidad), Function training (Entrenamiento funcional).

This sequence seeks to establish a solid foundation for effective and specific muscle activation[62].

In the initial stages of the process —Finding and Feeling—, it is essential to correctly identify the pelvic floor muscles (PFM) and develop the necessary body awareness to perceive their contraction in isolation. In accordance with the principles of physiological muscle training aimed at developing —Strength — and functionality, the exercises should consist of maximum, selective, and repetitive voluntary contractions, accompanied by adequate periods of relaxation between each contraction. To —Continue toward functionality —, regular training is required, often over a prolonged period of time.

The main challenge for the pelvic physiotherapist is to integrate functional training effectively, allowing the patient to experience early improvement in symptoms. This —Functional training— involves reproducing, during rehabilitation, everyday situations in which the patient used to experience incontinence, thus promoting automatic and effective activation of the MSPs. Once this objective has been achieved, motivation and adherence to treatment follow.

A publication in 2021 (Del Forno et al.) investigated the main pelvic symptoms and pelvic floor muscle dysfunction in women with deep infiltrating endometriosis (DIE). The study concluded that all patients had symptoms of dysmenorrhea, chronic pelvic pain, dyspareunia, dysuria, dyschezia, and vulvodynia. Muscle dysfunction characterized by hypertonicity, the presence of myofascial trigger points, decreased contractile capacity, and difficulty achieving adequate relaxation of the pelvic floor muscles was also evident. In addition, symptoms associated with abdominal muscle pain and muscle shortening in the lower extremities were reported.

Transperineal ultrasound was used to analyze the levator ani hiatus (LAH) area during the Valsalva maneuver in patients with IPP. The main objective was to determine the effect of pelvic floor physical therapy in women with superficial dyspareunia.

After five physiotherapy treatment sessions, three-dimensional (3D/4D) transperineal ultrasound showed an increase in the LHA area during the Valsalva maneuver, accompanied by clinical improvements in superficial dyspareunia, chronic pelvic pain, and the ability to relax the pelvic floor muscles[63].

Neuromodulation

Neuromodulation of the posterior tibial nerve is an option for patients with pelvic pain, chronic pain, dyspareunia, and deep endometriosis. It has been shown to significantly reduce stress and improve quality of life, as well as sexual function in EHP-30. It is a minimally invasive technique that responds to nerve blockage, with mild side effects, and can be self-administered. The application of neuromuscular stimulation has detected significant improvements after 10 weeks of treatment with a frequency of 2 to 100Hz for 30 minutes per session, once a day, 3 sessions a week, significant changes in pain measurement on the numerical scale, endometriosis symptom severity scale, and SF-36[26,64].

Tens

This is a type of non-invasive, low-cost, and easily accessible analgesic current used for pain treatment, which acts by blocking the spinal cord and releasing endogenous opioids, thereby reducing

pain perception. It is applied using a device that sends low-intensity electrical currents in two delivery formats: superficial and transcutaneous. Its application in patients with endometriosis has proven effective as a complementary treatment for the modulation of deep and superficial pelvic pain (dyspareunia), contributing to an improvement in the quality of life of those who use this tool[65].

Myofascial release

Musculoskeletal pain is one of the most common causes of chronic pain, accounting for up to 56% of cases in people over 35 and up to 86% of cases in people over 56[66].

Myofascial pain syndrome (MPS) is a regional pain condition localized in a muscle or functional muscle group, characterized by trigger points located on muscle bands that are tense to the touch, evoking sensory symptoms and generating referred pain.

Interventions such as physical therapy, education, behavior modification, neuromuscular retraining, transcutaneous electrical stimulation, auditory or visual biofeedback (intravaginal or intrarectal with Kegel exercises), and the development of a home exercise plan, manual release of myofascial points with vaginal or anal massage, do not have conclusive evidence, However, in cases of coexisting vulvodynia, the application of cold or heat through hot baths, towels on the skin, or cold packs may be useful.

Exercise

Exercise is part of the non-pharmacological treatment of patients with chronic pelvic pain. International clinical guidelines suggest that patients with endometriosis engage in regular physical activity, as it has a beneficial impact on aspects such as symptom reduction, improved pain perception, and quality of life. The available literature suggests the application of personalized and supervised exercise guidelines, over a minimum period of 8 weeks, that include aerobic exercise routines, flexibility exercises, and relaxation exercises[67].

In addition, regular exercise has been shown to be a protective factor in people with chronic inflammatory diseases because it increases systemic levels of anti-inflammatory cytokines[65].

The various therapeutic techniques described play a fundamental role in the rehabilitation of patients with endometriosis, both operated and non-operated. These interventions contribute significantly to the management of chronic pain, the release of post-surgical adhesions, physical reconditioning, and pelvic floor strengthening. Together, they improve patients' quality of life and offer an accessible, low-cost therapeutic alternative, promoting a comprehensive and personalized approach to this condition.

Psychological management of endometriosis

It is necessary to raise awareness of the importance of a multidisciplinary approach to the treatment of endometriosis, taking into account the psychological aspect[68].

This approach should be initiated early, as it lays the foundation for proper evaluation and selection of a treatment from which the patient can benefit[69]. However, experience shows that its incorporation requires psychoeducation by the treating physician to clarify the purpose of mental health support. Addressing psychological aspects early on involves offering the patient opportunities to accept her illness, activate coping resources such as pain self-management[70], set realistic expectations for treatment, and receive support in important decisions, such as fertility issues.

The experience of living with endometriosis is often associated with a psychological state characterized by a sense of threat to integrity, feelings of helplessness due to previous therapeutic failures, and a perception of exhaustion of personal and psychosocial resources. Women with this condition report alterations in their feminine identity[71], difficulties with self-image, feelings of being a burden, along with symptoms of anxiety and depression, which negatively affect their psychological health and impact their interpersonal relationships and quality of life[72,73,74,75,76].

The first step in this approach is a psychological evaluation, where a safe space can be created for women to share their concerns, fears, and emotional challenges related to endometriosis. It is necessary to adapt tests that assess the psychological impact[77], which should be perfor-

med by a professional in the field, with special attention to the psychosocial factors involved.

Understanding how the patient experiences her illness facilitates understanding what it means to her, the emotions associated with it, her coping style, and her willingness to change. Assessing behavior—such as decreased physical activity, sensory deprivation, drowsiness, and listlessness—is key, as these behaviors can lead to isolation and restricted social participation.

In the workplace, the study by Baciu et al. (2021) indicates that there is an impact on self-esteem and self-confidence, as symptoms limit daily activities such as working or participating socially. Therefore, it is important to assess their interpersonal relationships and perceived support, considering that absenteeism or frequent complaints can generate conflictive dynamics that lead to work stress or perceptions of rejection and discrimination[78].

At the family level, the attitude of the environment towards illness and disability should be assessed, evaluating behavior patterns and the quality of support. It is also important to consider the possible impact in this area due to the presence of anhedonia, which can lead to social avoidance[79].

In romantic relationships, it is essential to investigate the impact of endometriosis, including its effect on sexuality, due to dyspareunia and other factors related to sexual functioning[72].

A basic tool in this assessment is the clinical psychological interview, which allows information to be obtained for a timely mental health diagnosis, exploring symptoms, emotional state, psychological resources, and adaptation. This comprehensive view of the patient is essential for implementing appropriate therapeutic strategies.

In addition to the interview, structured psychological tests may be included.

Given that this disease involves challenges for adaptation, self-care, and treatment adherence, several authors recommend using quality of life measurement instruments, such as the SF-12 or the Endometriosis Health Profile-5[6].

Women with endometriosis and chronic pain often experience distress, sleep disturbances, irritability, and hopelessness, which profoundly affects their quality of life[76].

Some psychological treatments are described below:

Pain education: This is essential for women to better understand their condition. It improves understanding, empowers them to make informed decisions, and promotes adherence to treatment. It involves constant dialogue, taking into account what the patient already knows and believes about her health. It reduces the stigma associated with chronic pain. This process goes beyond providing information; it requires clinical sensitivity to respond to the patient's emotional feedback and understand that not everyone reacts the same way to the unknown.

By better understanding pain, patients can reduce the fear and anxiety associated with it. In addition, this educational approach can encourage the patient's active participation in their own pain management[80].

Breathing and muscle relaxation strategies: Breathing and relaxation can be useful tools. Techniques such as progressive muscle relaxation and diaphragmatic breathing aim to reduce the tension and physiological arousal associated with stress. These strategies have been shown to be effective in both acute and chronic pain syndromes.

Cognitive-behavioral therapy (CBT): This aims to identify and modify maladaptive behaviors and dysfunctional thought patterns (distorted beliefs, catastrophic thinking, prejudices). In endometriosis, these beliefs may be related to female identity and motherhood. Beliefs such as that women without children are less socially valued or defective have been found in women with endometriosis[6,75].

CBT also works on:

- Recognizing ambivalence in the face of change.
- Cognitive flexibility (modifying beliefs and biases).

- Identifying factors that trigger and maintain stress.

- Restructuring irrational thoughts.

Mindfulness: Mindfulness-based interventions have been shown to be effective in improving pain self-regulation, associated mood disorders, and stress reduction.

Family interventions: Endometriosis can affect not only the individual, but also their family and close relationships. Including the family in the therapeutic process can improve emotional well-being, strengthen the sense of support, and reduce critical attitudes toward the patient. The physical limitations imposed by endometriosis can alter family dynamics, requiring adjustments in roles, responsibilities, and shared activities[72].

Discussion

A comprehensive, patient-centered approach.

Pain management in women with endometriosis may require comprehensive care from a multidisciplinary team that includes psychologists, physical therapists, gastrointestinal and nutritional specialists, pain therapists, surgeons, and specialists in gynecology and reproductive medicine, among others.

Avoiding the use of ineffective hormonal treatments, as well as unnecessary and potentially risky surgical procedures, should always be a matter for in-depth analysis when choosing the best option for these patients.

It is essential to understand the needs and preferences of each woman with endometriosis in order to increase her ability to cope with the disease and improve treatment compliance. Factors such as being listened to and understood, receiving simple and clear explanations, and participating in medical decisions increase confidence in the medical teams in charge of her care.

Conclusion

The therapies outlined in this review have demonstrated effectiveness in controlling the symptoms of endometriosis, particularly pain; however, they do not cure the disease, and symptoms often recur once treatment is discontinued. Conversely, although surgery may also alleviate pain and improve fertility, it entails substantial risks and does not consistently prevent recurrence.

Therefore, in many cases, a combination of the therapeutic modalities discussed will be recommended, including for long-term use following surgery, with the aim of maximizing their effectiveness in controlling pain and, collectively, reducing the risk of recurrence.

Being able to offer varied and complementary options for the management of symptomatic endometriosis, with a comprehensive and patient-centered approach, will allow us to achieve adequate and consistent results over time.

References

1. Organización Mundial de la Salud. Notas descriptivas/ Detalle/ Endometriosis. 24 de marzo 2023.
2. Rossell EL, Plana- Ripoll O , Josiasen M, et al. Association between endometriosis and working life in Danish Women. Human Reproduction, 2025, 40(3), 461–468
3. Bell RJ, Robinson PJ, Skiba MA, et al. The impact of endometriosis on work ability in young Australian women. Aust N Z J Obstet Gynaecol, 2023;63:556–563.
4. Soliman AM, Coyne KS, Gries KS, et al. The effect of endometriosis symptoms on absenteeism in the workplace and at home. J Manag Care SpecPharm, 2017;23:745–754.
5. Armour M, Sinclair J, Ng CHM, Hyman MS, Lawson K, Smith CA, et al. Endometriosis and chronic pelvic pain have similar impact on women, but time to diagnosis is decreasing:an Australian survey. Sci Rep. 2020; 10:16253.
6. Orientaciones técnicas para la atención de integral de la endometriosis. Programa Nacional de Salud de la Mujer. Departamento de Ciclo Vital, División de Prevención y Control de Enfermedades. Ministerio de Salud (MINSAL); 2024.
7. Asociación Internacional para el Estudio del Dolor (IASP). Classification of Chronic Pain [Internet]. 2020. Disponible en: https://www.iasp-pain.org
8. Ben Rimón S. Neuropathic Pain in Endometriosis: Mechanisms and Management. J Pain Res. 2018;11:2549-2557.
9. Cervero F, Laird JMA. Nociplastic Pain: From Mechanism to Treatment. Pain. 2018;159(1):S1-S10.
10. Vidoris P, et al. Combination Therapy with NSAIDs and Paracetamol in Chronic Pain Management: A Systematic Review. Pain Med. 2021;22(3):567-576.
11. Bachmann F, et al. Opioid Use in Chronic Pain: Risks and Benefits. J Clin Med. 2019;8(6):823.

12. Liu X, et al. Gabapentin and Pregabalin in Neuropathic Pain: A Comparative Review. Pain Pract. 2022;22(1):45-56.
13. Rogers AH, et al. Antidepressants in Chronic Pain Management: A Review of Evidence. J Pain Res. 2020;13:307-316.
14. Smith R, et al. Omega-3 Fatty Acids and Inflammation: Implications for Chronic Pain Management. Nutrients. 2020;12(9):2774.
15. Dean C, et al. Magnesium Citrate in Chronic Pain: A Systematic Review and Meta-Analysis. J Integr Med. 2017;15(5):341-349
16. Visser E, et al. Ketamine as a treatment for neuropathic pain. Pain Med Rev. 2015;18(2):112-119.
17. Cohen SP, et al. Consensus guidelines on the use of intravenous ketamine infusions for acute pain management. Pain Med. 2018;19(4):977-996.
18. Singh JB, et al. Ketamine as a treatment of complex regional pain syndrome in adults . J Pain. 2020:21(3):3-14
19. O'Connor M, et al. Clinical use of ketamine for chronic pain management: A review. Curr Pain Headache Rep. 2017;21(1):13-25.
20. Challapalli V, et al. Systematic review of intravenous lidocaine for neuropathic pain. Curr Pain Headache Rep. 2005;9(3):214-221.
21. Tremont-Lukats IW, et al. Systemic administration of local anesthetics to relieve neuropathic pain: a systematic review and meta-analysis. Pain Physician. 2006;9(1):29-50.
22. De Oliveira CM, et al. Intravenous lidocaine and magnesium for management of chronic pain and comorbid depression in a patient with refractory chronic pain. Pain Pract. 2014;14(5):361-365.
23. Plancarte R, et al. Superior hypogastric plexus block for pelvic cancer pain. Anesth Analg. 1990;70(3):291-294.
24. Ho KH, et al. Ganglion impar block for visceral and sympathetically mediated pain: A technical report. Pain Med. 2012;13(1):35-39.
25. Baranowski AP, et al. Pudendal nerve blocks for pelvic pain. Int Urogynecol J. 1999;10(4):250-252.
26. European Society of Human Reproduction and Embryology (ESHRE). Endometriosis Guideline. 2022.
27. Velja Mijatovic, Paolo Vercellini, Towards comprehensive management of symptomatic endometriosis: beyond the dichotomy of medical versus surgical treatment, Human Reproduction, Volume 39, Issue 3, March 2024, Pages 464–477, https://doi.org/10.1093/humrep/dead262
28. Jensen JT, Schlaff W, Gordon K. Use of combined hormonal contraceptives for the treatment of endometriosis-related pain: a systematic review of the evidence. Fertil Steril 2018;110: 137-152.e131.
29. Grandi G, Barra F, Ferrero S, Sileo FG, Bertucci E, Napolitano A, Facchinetti F. Hormonal contraception in women with endometriosis: a systematic review. Eur J Contracept Reprod Health Care 2019;24:61–70.
30. Muzii L, Di Tucci C, Achilli C, Di Donato V, Musella A, Palaia I, Panici PB. Continuous versus cyclic oral contraceptives after laparoscopic excision of ovarian endometriomas: a systematic review and metaanalysis. Am J Obstet Gynecol 2016;214: 203-211.
31. Mitchell JB, Chetty S, Kathrada F. Progestins in the symptomatic management of endometriosis: a meta-analysis on their effectiveness and safety. BMC Womens Health 2022;22:526.
32. Canis M, Guo SW. In the thicket of fears, doubts, and murky facts: some reflections on treatment modalities for endometriosis-associated pain. Hum Reprod. 2023 Jul 5;38(7):1245-1252. doi: 10.1093/humrep/dead061. PMID: 37023473.
33. Petraglia F, Hornung D, Seitz C, Faustmann T, Gerlinger C, Luisi S, Lazzeri L, Strowitzki T. Reduced pelvic pain in women with endometriosis: efficacy of long-term dienogest treatment. Arch Gynecol Obstet 2012;285: 167-173.
34. Strowitzki T, Faustmann T, Gerlinger C, Seitz C. Dienogest in the treatment of endometriosis-associated pelvic pain: a 12-week, randomized, double-blind, placebo-controlled study. Eur J Obstet Gynecol Reprod Biol 2010;151: 193-198.
35. Momoeda M, Harada T, Terakawa N, Aso T, Fukunaga M, Hagino H, Taketani Y. Long-term use of dienogest for the treatment of endometriosis. J Obstet Gynaecol Res 2009;35: 1069-1076.
36. Laura K, Katharina D, Committee obotG. Diagnosis and management of endometriosis: summary of NICE guidance. BMJ. 2017;358:j4227.
37. Tanmahasamut P, Rattanachaiyanont M, Angsuwathana S, Techatraisak K, Indhavivadhana S, Leerasiri P. Postoperative Levonorgestrel-Releasing Intrauterine System for Pelvic Endometriosis-Related Pain: A Randomized Controlled Trial. Obstetrics & Gynecology. 2012;119(3).
38. Margatho D, Carvalho NM, Bahamondes L. Endometriosis-associated pain scores and biomarkers in users of the etonogestrel-releasing subdermal implant or the 52-mg levonorgestrel-releasing intrauterine system for up to 24 months. Eur J Contracept Reprod Health Care 2020;25: 133-140.
39. Brown J, Crawford TJ, Datta S, Prentice A. Oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev. 2018;5(5):CD001019-CD.
40. Collinet P, Fritel X, Revel-Delhom C, Ballester M, Bolze PA, Borghese B, et al. Management of endometriosis: CNGOF/HAS clinical practice guidelines - Short version. J Gynecol Obstet Hum Reprod. 2018;47(7):265-74.
41. Donnez J, Dolmans M-M. Endometriosis and Medical Therapy: From Progestogens to Progesterone Resistance to GnRH Antagonists: A Review. J Clin Med. 2021;10(5):1085.
42. Wu D, Hu M, Hong L, Hong S, Ding W, Min J, et al. Clinical efficacy of add-back therapy in treatment of endometriosis: a meta-analysis. Archives of Gynecology and Obstetrics. 2014;290(3):513-23.
43. Osuga Y, Ross D, Saul L, et al. Relugolix Combination Therapy for Women with Endometriosis-Associated Pain: Two Randomized Controlled Trials. Lancet. 2021;397(10260):1230–1240. DOI: 10.1016/S0140-6736(21)00527-9
44. Donnez J, Taylor HS, Taylor RN, et al. Linzagolix, an Oral GnRH Antagonist for the Treatment of Endometriosis-Associated Pain: Results from Two Phase 3 Randomized Controlled Trials (PRIMROSE 1 and 2). Fertil Steril. 2022;118(4):658–671. DOI: 10.1016/j.fertnstert.2022.06.011
45. Brown J, Pan A, Hart RJ. Danazol for pelvic pain associated with endometriosis. Cochrane Database Syst Rev. 2010;(12):CD000068.

46. Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol. 2014;10(5):261–275.

47. Ferrero S, Gillott DJ, Venturini PL, Remorgida V. Use of aromatase inhibitors to treat endometriosis-related pain symptoms: a systematic review. Reprod Biol Endocrinol 2011;9: 89.

48. Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, Heikinheimo O, Horne AW, Kiesel L, Nap A et al. ESHRE guideline: management of women with endometriosis. Hum Reprod 2014;29: 400-412

49. Chen I, Veth VB, Choudhry AJ, Murji A, Zakhari A, Black AY, Agarpao C, Maas JW. Pre- and postsurgical medical therapy for endometriosis surgery. Cochrane Database Syst Rev 2020;11: Cd003678.

50. Cevik EC, Taylor HS. Progestin induced depression in endometriosis. Fertil Steril. 2025 Jun;123(6):1155. doi: 10.1016/j.fertnstert.2025.02.033. Epub 2025 Feb 26. PMID: 40021037.

51. Cevik EC, Taylor HS. Mood lability and depression limit oral contraceptive therapy in endometriosis. Fertil Steril. 2025 May;123(5):838-845. doi: 10.1016/j.fertnstert.2024.12.011. Epub 2024 Dec 12. PMID: 39672361.

52. Vercellini P, Buggio L, Berlanda N, Barbara G, Somigliana E, Bosari S. Estrogen-progestins and progestins for the management of endometriosis. Fertil Steril 2016;106:1552–1571.e2.

53. Vercellini P, Buggio L, Somigliana E. Role of medical therapy in the management of deep rectovaginal endometriosis. Fertil Steril 2017;108:913–930.

54. Vercellini P, Buggio L, Frattaruolo MP, Borghi A, Dridi D, Somigliana E. Medical treatment of endometriosis-related pain. Best Pract Res Clin Obstet Gynaecol 2018b;51:68–91.

55. Vercellini P, Buggio L, Borghi A, Monti E, Gattei U, Frattaruolo MP. Medical treatment in the management of deep endometriosis infiltrating the proximal rectum and sigmoid colon: a comprehensive literature review. Acta Obstet Gynecol Scand 2018a;97:942–955

56. Vercellini P, Sergenti G, Buggio L, Frattaruolo MP, Dridi D, Berlanda N. Advances in the medical management of bowel endometriosis. Best Pract Res Clin Obstet Gynaecol 2021;71:78–99.

57. Thurnherr N, Burla L, Metzler JM, File B, Imesch P. Attitudes and perceptions of affected women towards endocrine endometriosis therapy: an international survey based on free-word association networks. Hum Reprod. 2024 Jan 5;39(1):83-92. doi: 10.1093/humrep/dead221. PMID: 37879845; PMCID: PMC10767788.

58. Fraga MV, Oliveira Brito LG, Yela DA, de Mira TA, Benetti-Pinto CL. Pelvic floor muscle dysfunctions in women with deep infiltrative endometriosis: an underestimated association. Int J Clin Pract. 2021;75(8):e14350. doi:10.1111/ijcp.14350.

59. Narayanan SP, Bharucha AE. A practical guide to biofeedback therapy for pelvic floor disorders. Curr Gastroenterol Rep. 2019;21(5):21. http://dx.doi.org/10.1007/s11894-019-0688-3

60. Roy H, Offiah I, Dua A. Neuromodulation for pelvic and urogenital pain. Brain Sci. 2018;8(10):180. doi:10.3390/brainsci8100180.

61. Bo K. Mechanisms for pelvic floor muscle training: morphological changes and associations between changes in pelvic floor muscle variables and symptoms of stress urinary incontinence and pelvic organ prolapse—a narrative review. Neurourol Urodyn. 2004;43(8):1977-96. doi:10.1002/nau.25551.

62. Berghmans B, Selcse M. The '5 E's' concept for pelvic floor muscle training: from finding the pelvic floor to functional use. J Womens Health Dev. 2021;4(6):630-635. doi:10.26502/jwhd.2644-28840024.

63. Del Forno S, Arena A, Pellizzone V, Lenzi J, Raimondo D, Cocchi L, et al. Assessment of levator hiatal area using 3D/4D transperineal ultrasound in women with deep infiltrating endometriosis and superficial dyspareunia treated with pelvic floor physical therapy. Ultrasound Obstet Gynecol. 2021 May;57(5):726-732. doi: 10.1002/uog.23590. PMID: 33428320.

64. Holly R, Ifeoma Offiah I, Dua A. Neuromodulation for pelvic and urogenital pain.Brain Sci. 2018;8(10):180. doi:10.3390/brainsci8100180.

65. Ticiana AA, Mira PC, Giraldo DA, Yela CL. Effectiveness of complementary pain treatment for women with deep endometriosis through Transcutaneous Electrical Nerve Stimulation (TENS): Randomized controlled trial. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2015;194:1–6.

66. Méndez Vega DA, Arce Gálvez L, Tovar Sanchez MA. Síndrome de dolor miofascial en la musculatura del suelo pélvico femenino. Revisión narrativa de la literatura. Rev Soc Esp Dolor. 2022;29(2):88-96. doi:10.20986/resed.2022.4109/2021.

67. Xie M, Qing X, Huang H, Zhang L, Tu Q, Guo H, et al. The effectiveness and safety of physical activity and exercise on women with endometriosis: A systematic review and meta-analysis. 2025;20(2):e0317820. http://dx.doi.org/10.1371/journal.pone.0317820

68. Corte, L., Di Filippo, C., Gabrielli, O., Reppuccia, S., La Rosa, V., Ragusa, R., Fichera, M., Commodari, E., Bifulco, G., & Giampaolino, P. (2020).
La carga de la endometriosis en la esperanza de vida de las mujeres: Una visión narrativa sobre la calidad de vida y el bienestar psicosocial. International Journal of Environmental Research and Public Health, 17(13), 4683. https://doi.org/10.3390/ijerph17134683

69. Rivera,H.&Ugalde,F. (2021).Endometriosis: Una visión detrás del estigma. Revista Ciencia y Salud Integrando Conocimientos, 5(4), 53–62. https://doi.org/10.34192/cienciaysalud.v5i4.308

70. Quintero,M.,Vinaccia,S.,&Quiceno,J.(2017). Endometriosis: Aspectos psicológicos. Revista Chilena de Obstetricia y Ginecología, 82(4), 447–452.

71. Márki, G., Vásárhelyi, D., Rigó, A., Kaló, Z., Ács, N., & Bokor, A. (2022). Desafíos y posibles soluciones para vivir con endometriosis: Un estudio cualitativo. BMC Women's Health, 22(20). https://doi.org/10.1186/s12905-022-01603-6

72. Aerts, L., Grangier, L., Streuli, I., Dällenbach, P., Marci, R., Wenger, J., & Pluchino, N.(2018). Impacto psicosocial de la endometriosis: De la comorbilidad a la intervención. Best Practice & Research Clinical Obstetrics & Gynaecology, 50, 2–10. https://doi.org/10.1016/j.bpobgyn.2018.01.008

73. Chandel, P., Maurya, P., Hussain, S., Vashistha, D., & Sharma, S. (2023). Endometriosis y depresión: Una doble agonía para las mujeres. Annals of Neurosciences, 30(3), 205–209. https://doi.org/10.1177/09727531231152022

74. Facchin, F., Barbara, G., Dridi, D., Alberico, D., Buggio, L., Somigliana, E., Saita, E., & Vercellini,P. (2017). Salud mental en mujeres con endometriosis: Búsqueda de predictores de distrés psicológico. Human Reproduction, 32(9), 1855–1861. https://doi.org/10.1093/humrep/dex249

75. Facchin, F., Buggio, L., Dridi, D., & Vercellini, P. (2021). El valor de una mujer: El impacto de las creencias sobre la maternidad, la identidad femenina y la infertilidad en mujeres sin hijos con endometriosis. Journal of Health Psychology, 26(7), 1026–1034. https://doi.org/10.1177/1359105319863093

76. Jones, G. L., Budds, K., Taylor, F., Musson, D., Raymer, J., Churchman, D., Kennedy, S. H., &Jenkinson, C. (2024). A systematic review to determine use of the Endometriosis Health Profiles to measure quality of life outcomes in women with endometriosis. Human Reproduction Update, 30(2), 186–214. https://doi.org/10.1093/humupd/dmad029

77. Schick, M., Germeyer, A., Böttcher, B., Hecht, S., Geiser, M., Rösner, S., Eckstein, M., Vomstein, K., Toth, B., Strowitzki, T., Wischmann, T., & Ditzen, B. (2022). El bienestar psicosocial de las parejas frente a la endometriosis. Health and Quality of Life Outcomes, 20(86). https://doi.org/10.1186/s12955-022-01991-1

78. Baciu, L., Irimie, A., Panaitescu, A., Peltecu, G., & Gica, C. (2021). Impacto psicológico de la endometriosis en la población urbana rumana. Revista de Mente y Ciencias Médicas, 8(16). https://doi.org/10.22543/7674.81.P120126

79. Mallorquí, A., Martínez-Zamora, M., & Carmona, F. (2022). Anhedonia en la endometriosis: Un síntoma inexplorado. Frontiers in Psychology, 13. https://doi.org/10.3389/fpsyg.2022.935349

80. Butler, D. S., & Moseley, G. L. (2017). Explain pain (2nd ed.). Noigroup Publications.

81. Smith, A. et al. (2023). Mindfulness-Based Interventions for Chronic Pain Management in Endometriosis: A Systematic Review. Journal of Alternative and Complementary Medicine, 29(5), 400-415.