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Endometriosis treatment in the 21st century: current trends and clinical perspectives

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ABSTRACT

Chronic pelvic pain, infertility, and severe menstrual symptoms are part of everyday life for millions of women around the world. These issues often remain undiagnosed, especially when it comes to endometriosis. Endometrioisis is a multifaceted disease that might be caused by hormonal imbalance, immune dysfunction, microbiome alterations and gene transformation. Managing endometriosis symptoms effectively is essential for patients' quality of life, fertility, and long-term health. In this review, we brought together current ideas on the treatment, considering both long-standing methods and novel approaches.

Keywords: endometriosis, hormonal therapy, microbiome, chronic pelvic pain, estrogen dependence

1. INTRODUCTION

Endometriosis is a chronic condition in which endometrial-like tissue grows outside of the uterus. Improper placement of the uterus lining cells leads to inflammation and the formation of scar tissue mostly in the pelvis region, which can cause severe chronic pelvis pain and infertility (Chapron et al., 2019).

The pathogenesis of endometriosis involves a variety of different factors, which proves the complexity of its treatment. The most conventional hypothesis is retrograde menstruation, which assumes that the endometrial fragments travel through the fallopian tubes (Vercellini et al., 2014). Some research highlighted that endometriosis is an estrogen-dependent and progesterone-resistant disease (Zhang & Wang, 2023), while other research points out the angiogenesis and neurogenesis dysregulation (Hey-Cunningham et al., 2013). A holistic approach is also gaining attention with recent studies about gut microbiota involved in pathogenesis (Guo & Zhang, 2024).

According to the data from the World Health Organization (WHO), endometriosis affects approximately 5-10% of women of reproductive age. It is essential to note that the true prevalence of endometriosis remains unknown, mainly due to the absence of a non-invasive diagnostic method (Shafrir et al., 2018). Late diagnosis remains a significant issue in the effective treatment of endometriosis and negatively impacts patients' quality of life. This review aims to raise awareness

about the complexity of endometriosis and present current treatment approaches. The increasing public and scientific recognition of endometriosis has sparked a new wave of research focused on developing more personalized strategies for patients with endometriosis.

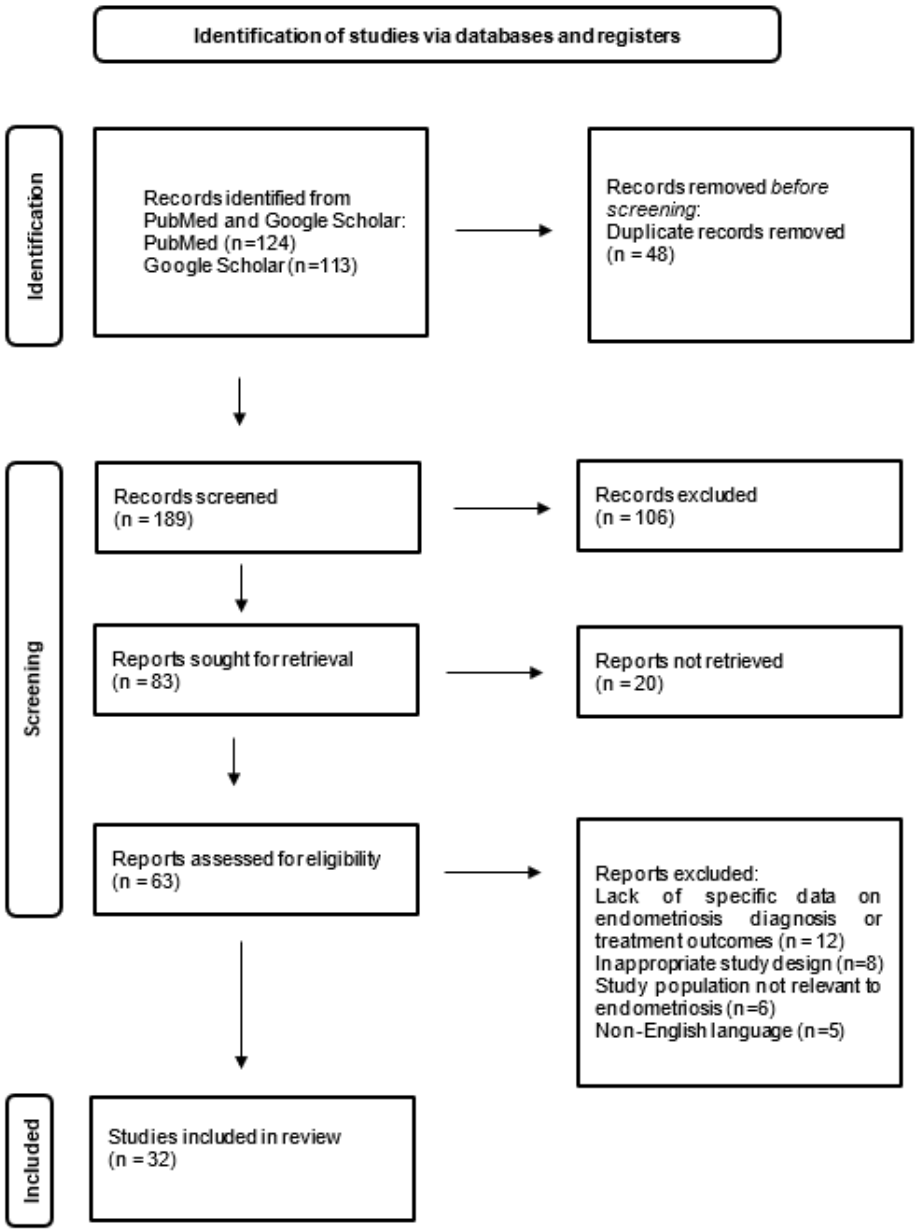

Figure 1: PRISMA flowchart

2. REVIEW METHODS

We reviewed studies from major scientific databases, including PubMed and Google Scholar, with a focus on endometriosis treatment. A total of 237 articles were identified through searches in selected databases. After removing 48 duplicates, 189 articles remained. After screening the titles and abstracts, we excluded 106 articles. The full text of 83 studies was sought for retrieval, and 20 of them were not retrieved. The full texts of 63 articles were then assessed for eligibility. Of these, 31 were excluded – 12 of this lack of specific data on endometriosis diagnosis or treatment outcomes, 8 of these had inappropriate study design, such as case reports, reviews without original data, or editorials, 6 of these were studies focused on populations not relevant to endometriosis and 5 of these were in languages other than English. Ultimately, 32 articles were included in this review (Figure 1). These selected articles were analyzed and

summarized in this review. We searched the databases using terms such as endometriosis, hormonal therapy, microbiome, chronic pelvic pain and estrogen dependence. We set the time range of published articles to January 2010- March 2025 and included some older publications if we considered them valuable for understanding the issue. All publications used in this review were written in English.

3. RESULTS AND DISCUSSION

Pathogenesis of Endometriosis

The cause of endometriosis is heterogeneous, as many different factors can contribute to its development. According to the most widely accepted model—the retrograde menstruation hypothesis—endometrial fragments travel through the fallopian tubes into the pelvic cavity, where they implant on the peritoneum and abdominal organs. There, they proliferate and trigger chronic inflammation, leading to the formation of adhesions (Vercellini et al., 2014). Elevated levels of pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α) and increased presence of activated macrophages and neutrophils have been identified in the peritoneal fluid of affected individuals (Yang et al., 2017; Zhang & Wang, 2023).

Another key feature of endometriosis is estrogen dependence and resistance to progesterone. Numerous studies have shown that the expression level of progesterone receptors, PR-A and PR-B, is generally lower in ectopic endometrial lesions (table 1). Simultaneously, high expression of estrogen receptors, especially Erβ, leads to the upregulation of aromatase activity and increased estrogen production within ectopic lesions (Zhang & Wang, 2023).

One of the key components of endometriosis pathogenesis is the dysregulation of angiogenesis and neurogenesis. Neurogenesis promotes nerve fiber growth around endometriosis lesions. It appears to play a central role in symptom manifestation as it is associated with chronic pelvic pain (Hey-Cunningham et al., 2013).

Recent studies suggest that the gut microbiota may be involved in the pathogenesis of endometriosis. Dysbiosis may contribute to systemic inflammation and immune dysregulation; however, the clinical significance of these findings requires confirmation through well-designed clinical studies (Guo & Zhang, 2024).

Table 1. Key Mechanisms Involved in the Pathogenesis of Endometriosis

Pathogenic Mechanism	Description	Key Molecules / Factors	Clinical Implication
Retrograde Menstruation	Backflow of menstrual blood carrying endometrial cells into the pelvic cavity	–	Initiates ectopic implantation
Inflammation	Activation of immune cells and production of pro-inflammatory cytokines	IL-1β, IL-6, TNF-α, macrophages, neutrophils	Promotes lesion survival and adhesion
Estrogen Dependence	Increased local estrogen production via aromatase upregulation	ERβ, Aromatase	Sustains lesion growth
Progesterone Resistance	Decreased response to progesterone due to reduced PR expression	PR-A, PR-B	Hinders anti-proliferative hormonal control
Angiogenesis	Formation of new blood vessels around lesions	VEGF	Supports lesion nourishment and growth
Neurogenesis	Growth of nerve fibers into endometrial lesions	Nerve growth factors	Contributes to chronic pelvic pain
Gut Microbiota Dysbiosis	Altered microbiome contributing to systemic inflammation and immune dysregulation	LPS, microbial imbalance	Emerging target; requires further investigation

Traditional Treatment Approaches

The traditional endometriosis treatment methods we are familiar with today primarily consist of pharmacological therapy and surgical interventions. The main goals of these methods are reducing the severity of the symptoms, slowing disease progression, and improving patients' quality of life.

Pharmacological Therapy

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Pain management is one of the most important goals of endometriosis treatment when trying to improve patients' quality of life. NSAIDs tend to be used as therapy of first choice due to their accessibility; however, some small research found minimal and low-quality evidence regarding their efficacy for this specific pain. Based on the available data from one small study, the review's authors could not definitively conclude if NSAIDs, specifically naproxen, effectively relieve endometriosis-related pain (Brown et al., 2017).

Hormonal Therapy

Due to the limited efficacy of NSAIDs in some patients, hormonal therapies remain the most effective way of symptom management. The primary focus of all hormonal treatments is to suppress or lower systemic estrogen levels by inhibiting the hypothalamic-pituitary-ovarian axis or by inducing pseudo-decidualization, leading to amenorrhea (Vannuccini et al., 2022).

Progestin-only pills and combined oral contraceptives (COCs) are typically used as first-line hormonal treatment as they are well-tolerated by patients and can be used for a long time. Progestins act through multiple mechanisms: anti-estrogenic, pro-apoptotic, anti-inflammatory, and anti-proliferative effects. Progestins suppress endometrial growth and exert antimitotic activity in endometriotic lesions. That mechanism ultimately leads to decidualization and atrophy of these lesions (Quaas et al., 2015; Gezer & Oral, 2015). All synthetic progestins achieve symptomatic improvement as they reduce endometriosis-associated pain in approximately 90% of the patients (Gezer & Oral, 2015).

Despite their efficacy, progestins are associated with several side effects. These are mainly due to their androgenic actions and include weight gain, acne, and menstrual irregularities. Long-term administration of progestin (depot medroxyprogesterone acetate; DMPA, also known as Depo-Provera) can be associated with a decrease in bone mineral density (Quaas et al., 2015). Levonorgestrel may cause side effects such as spotting, breakthrough bleeding, bloating, weight gain, and headache in up to one-third of patients. Lynestrenol was responsible for hot flushes, acne, and sweating, which were the main problems reported by up to 59% of patients. (Gezer & Oral, 2015).

GnRH Agonists and Antagonists

Given that endometriosis is an estrogen-dependent disease, gonadotropin-releasing hormone (GnRH) agonists have become an established option in its treatment. GnRH agonists, such as leuprolide acetate and gosereline, work by reducing GnRH pulsatility, which in turn suppresses the gonadotropic axis and prevents estrogen stimulation of ectopic glands. This mechanism leads to estrogen levels like those seen post-menopause, which avoid stimulation of the uterus lining. This significant reduction in estrogen can lead to progressive bone loss and severe vasomotor symptoms (Brichant et al., 2021).

To overcome some of the limitations associated with GnRH agonists, GnRH antagonists have been developed as an alternative approach with a more favorable side effect profile. These agents, such as cetrorelix and elagolix, primarily work by completely blocking the GnRH receptor, thereby suppressing GnRH-mediated signal transduction. As a result, they reduce gonadotropin secretion (Ortmann et al., 2002). Due to their direct antagonist action, they avoid triggering the flare-up effect that would cause a rapid suppression of gonadotropin secretion (Capezzuoli et al., 2022).

Surgical Treatment

Surgical excision is the only cytoreductive approach with promising symptom-relief rates. The basic principles of endometriosis excisional operation involve the uncomplicated resection of visualized endometriotic lesions, performing adhesiolysis, and restoring the normal pelvic anatomy. Surgical intervention is often necessary when organ damage is suspected or has already been detected (Ferrari et al., 2024).

Minimally invasive surgery (MIS), particularly laparoscopy, is currently the approach of choice for endometriosis surgery. This technique offers variety of advantages that it became a gold standard in treatment. Clinicals observe benefits such as smaller blood loss,

decreased pain after the surgery, and shorter duration of hospitalization (Ferrari et al., 2024). Laparoscopic technique of endometriosis surgery is beneficial for better postoperative pain sensation and fertility (table 2). It is also considered safe and efficient for treating deep endometriosis with visceral localization, such as in the urinary tract and colon or rectum (Ferrari et al., 2024).

Table 2. Traditional Endometriosis Treatment Approaches

Treatment Type	Method	Mechanism of Action	Advantages	Disadvantages / Side Effects
Pharmacological	**NSAIDs**	Inhibition of prostaglandin synthesis (anti-inflammatory and analgesic effects)	Widely accessible, rapid symptom relief	Limited evidence of efficacy in endometriosis-specific pain
	Progestins / COCs	Estrogen suppression, anti-inflammatory and antiproliferative effects	Effective in reducing pain and controlling menstruation	Androgenic effects (acne, weight gain), menstrual irregularities
	GnRH Agonists	Suppress HPO axis → reduce estrogen levels	Effective in moderate to severe cases	Menopausal-like symptoms, bone density loss
	GnRH Antagonists	Direct GnRH receptor blockade without initial "flare-up" effect	Fewer side effects than agonists, faster onset	Possible hypoestrogenic symptoms with long-term use
Surgical	**Laparoscopy (MIS)**	Lesion excision, adhesiolysis, pelvic anatomy restoration	Improves fertility, reduces pain, short recovery time	Risk of recurrence, requires surgical expertise
	Advanced Surgery (e.g., Laparotomy)	Resection of deeply infiltrating endometriosis, organ reconstruction	Effective in complex cases involving bowel or urinary tract	Higher risk of complications, longer hospitalization

Emerging and Experimental Therapies

Modern Hormonal Therapies

Oral gonadotropin-releasing hormone (GnRH) receptor antagonists represent a significant improvement in managing endometriosis-associated pain. The main disadvantage of elagolix, particularly at higher effective doses, is its association with hypoestrogenic side effects, such as hot flushes and a clinically significant reduction in bone mineral density (BMD). These adverse effects mean a maximum treatment duration limit, typically 6 months for the high-dose regimen and up to 24 months overall, due to concerns about bone density loss (Ortmann et al., 2002).

Relugolix combination therapy (relugolix 40 mg, estradiol 1 mg, and norethisterone acetate 0.5 mg) was explicitly developed as a treatment to overcome these long-standing challenges. While relugolix monotherapy, like other GnRH antagonists, leads to dose-dependent decreases in BMD and increases in vasomotor symptoms (Osuga et al., 2021; Giudice et al., 2022), the combination therapy was developed to reduce the effects of hypoestrogenism. Clinicians observed that relugolix could maintain estradiol concentrations within a therapeutic range, thereby providing pain relief while minimizing side effects. This approach allows for the potential for long-term use (Osuga et al., 2021).

Another novel gonadotropin-releasing hormone (GnRH) receptor antagonist that has shown promising results in endometriosis-associated pain treatment is Linzagolix. The main advantage of this agent is precise control over estrogen levels, as it allows to keep the range of 20–60 pg/mL. It is beneficial because this range allows for the reduction of symptoms associated with endometriosis while minimizing side effects, such as loss of bone mineral density (BMD) (Donnez et al., 2023). Furthermore, linzagolix shows a rapid onset of therapeutic effects. It quickly reduces estradiol concentrations, resulting in fast symptom relief. The response was defined as at least a 30% reduction in menstrual dysmenorrhea and non-menstrual pelvic pain severity combined. Specifically, response rates were 61.5% with 75 mg linzagolix and 56.3% with 200 mg linzagolix, compared to 34.5% with placebo (Donnez et al., 2023). Aside from pain reduction, linzagolix was also proven to reduce difficulty associated with defecation and improve overall patient well-being, which was measured by quality-of-life scales. These benefits are maintained or further improved through 52 weeks of continuous administration. In the Phase 3 EDELWEISS 3 clinical trial, testing two regimens—75 mg without hormonal add-back therapy (ABT) and 200 mg with hormonal ABT—the 200 mg regimen with hormonal ABT successfully alleviated menstrual dysmenorrhea and non-menstrual pelvic pain within 3 months of therapy. Notably, by 52 weeks, both the 200 mg dose with ABT and the 75 mg dose reduced both types of pain, making linzagolix a promising agent for managing endometriosis pain (Donnez et al., 2023).

Selective Estrogen Receptor Modulators (SERMs) represent a new group of agents that have recently gained attention in the endometriosis treatment as they can modulate estrogen activity without reducing estrogen levels. SR-16234 is a novel SERM that is structurally different from previously approved SERMs. It has been reported to have estrogen receptor α antagonistic activity and weak partial agonistic activity to the β receptor (Harada et al., 2018).

A study conducted by Harada et al., (2018) evaluated SR-16234 in ten patients with dysmenorrhea and pelvic pain related to endometriosis and adenomyosis, who received 40 mg of SR-16234 once a day for 12 weeks. The trial results indicated statistically significant improvements, as pelvic pain VAS significantly decreased at 4, 8, and 12 weeks compared to baseline. Objective observations, such as stiffness of Douglas' pouch and restricted uterine mobility, showed reduced severity after treatment. In one patient, a chocolate cyst with a volume of 13,305 mm^3 decreased to 1,914 mm^3 by 8 weeks and disappeared at 12 weeks. Moreover, mean endometrial thickness decreased from 9.75 mm at baseline to 6.87 mm at 12 weeks in 8 patients. The sources highlight that SR-16234 appears to have a more favorable side effect profile compared to other common endometriosis treatments due to its "purer ERα antagonist tendencies".

A small study conducted by Kulak et al., (2011) evaluated the administration of 3 mg/kg·d of the SERM Bazedoxifene (BZA) to mice with experimental endometriosis for 8 weeks. The study showed that BZA blocked estrogen-induced stimulation of the endometrial tissue while preserving its effects on bone and the central nervous system (Table 3).

Table 3. Novel Hormonal Therapies for Endometriosis

Therapy	Mechanism	Benefits	Limitations / Notes
Elagolix	Oral GnRH antagonist → lowers estrogen	Effective pain relief	Hypoestrogenic effects; BMD loss; limited long-term use
Relugolix combination therapy	GnRH antagonist + estrogen + progestin	Maintains therapeutic estrogen window; fewer vasomotor & bone effects	Long-term safety still under evaluation
Linzagolix	Dose-dependent estrogen suppression	Rapid symptom relief; preserves BMD; long-term efficacy (up to 52 weeks)	Phase 3 data promising but still under regulatory assessment
SR-16234 (SERM)	ERα antagonist, weak ERβ agonist	Pain reduction, endometrial thinning, fewer side effects	Early-stage clinical data
Bazedoxifene (BZA)	SERM blocking estrogen	Maintains bone/CNS health in	Preclinical stage

	stimulation in endometrium	animal models	

Modern Endometriosis-Associated Pain Management

Conventional pharmacological treatments are associated with limited effectiveness and adverse side effects. Clinical studies have shown that Sacral Neuromodulation (SNM) can significantly reduce chronic pelvic pain. A systematic review and meta-analysis of 20 studies conducted by Greig et al., (2023) found a weighted mean difference in pain scores on a 10-point scale of -4.64 (95% confidence interval [CI] = -5.32 to -3.95, $p < 0.00001$). This difference indicates a substantial improvement in pain scores, with reported improvements ranging from 40% to 53% in patients who received a complete implant. All studies that assessed quality of life reported improvements in various QoL domains following SNM treatment. Specifically, areas like bodily pain, physical function, social function, physical role, general health, mental health, and vitality showed improvement. The significant benefit of SNM in pain reduction is maintained at 6, 12, and 24 months, with some studies reporting continued considerable decrease in pain scores up to 5 years (Greig et al., 2023).

Transcranial Direct Current Stimulation (tDCS) is a non-invasive brain stimulation technique that utilizes electrodes placed on the scalp to deliver a weak electric current, thereby modulating neuronal activity (Thair et al., 2017). A randomized controlled clinical trial conducted by Mechsner et al., (2023) demonstrated that this technique significantly decreased pain severity in patients with endometriosis and chronic pelvic pain. The group using tDCS showed a pain level reduction of approximately 41.3% on the NRS compared to the placebo group (table 4). Moreover, pain perception remains lower even after 1 week after stimulation. This suggests that the tDCS technique may be beneficial for long-term use.

Table 4. Modern Pain Management Techniques for Endometriosis

Technique	Mechanism	Benefits	Limitations / Notes
Sacral Neuromodulation (SNM)	Electrical stimulation of sacral nerves	Reduces pain (up to 53%); QoL improvements maintained up to 5 years	Invasive procedure; device-dependent
tDCS	Non-invasive brain stimulation via scalp electrodes	~41% pain reduction; long-lasting analgesic effects	Requires further clinical trials; access to technology

Immunomodulatory and Anti-Inflammatory Therapies

Immunological factors significantly play a significant role in the pathogenesis of endometriosis. Immunotherapy has become a promising innovative treatment strategy.

One type of the immunotherapy involves targeting the function of immune cells, particularly macrophages. The decrease in macrophage phagocytosis in peritoneal fluid is a significant contributor to immune imbalance in endometriosis patients. High expression of CD47, which provides a "don't eat me" signal, is increased in ectopic endometrium, blocking normal macrophage phagocytosis. Blocking the CD47-SIRPa signaling pathway reduces CD47 expression and allows macrophages to perform normal phagocytosis (Li et al., 2023).

Immunotherapy targeting the CD47-SIRPα signaling pathway appears to be effective for treating endometriosis. Another immunotherapy line used in endometriosis treatment is Immune Cytokine Modulators. Interleukins, especially IL-12, take part in the pathogenesis of endometriosis. IL-12 affects variety of factors regarding immunology. It stimulates the production of another cytokines, support the migration of inflammatory cells, and boost the cytotoxic activity of natural killer (NK) cells (Li et al., 2023). A study performed by Zhang et al., (2025) revealed that treatment of NK cells with an IL-12 heterodimer reduced the ratio of free p40 to IL-12. This action enhanced the cytotoxicity of NK cells in ectopic endometrial tissue, thereby suppressing the development of the ectopic endometrial tissue (table 5). It appears that IL-12 may be a potential target for reducing free p40 levels observed in patients with endometriosis.

Table 5. Immunomodulatory and Anti-inflammatory Therapies for Endometriosis

Therapy	Mechanism	Benefits	Limitations / Notes
CD47 blockade	Enhances macrophage phagocytosis of ectopic tissue	Targets immune dysfunction underlying disease	Experimental; preclinical models
IL-12 therapy	Enhances NK cell activity & suppresses ectopic tissue via cytokine modulation	Promotes immune clearance of lesions	Needs further human studies

Non-pharmacological and Supportive Therapies

Recent studies have examined the role of the gut microbiome as a potential new avenue for the treatment of endometriosis. Modulating the type and abundance of gut microbiota using probiotics has shown promising effects (Sahin et al., 2018). For instance, the strain *Lactobacillus gasseri* OLL2809 activates the NK cells, which were proven to suppress the growth of endometriosis lesions in mouse models. *L. Gasseri* could reduce chronic pelvic pain and dysmenorrhea in patients with endometriosis, while still being a safe treatment option (Sahin et al., 2018; Kobayashi, 2023).

Omega-3 PUFAs were proven to reduce LPS-producing bacteria (*E. coli*) and increase LPS-suppressing bacteria (Bifidobacterium). It led to a reduction in inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Moreover, premenopausal women taking Omega-3 fatty acids were less likely to develop endometriosis. Supplementation with alpha-linolenic acid (ALA), an omega-3 PUFA was proven to positively influence gut microbiota - it positively changed gut bacteria composition (*Lactobacillus, Bacteroides, Muribaculum, and Bifidobacterium*). Moreover, ALA reduced abdominal LPS levels and PGE2 concentrations (Guo & Zhang, 2024).

Another modern endometriosis treatment line is fecal microbiota transplantation (FMT). It is a procedure that involves administration of a fecal bacteria from a healthy donor into the gastrointestinal tract of a recipient. Experimental studies have shown that fecal microbiota transplantation from mice with endometriosis can increase lesion growth when transferred to the healthy one (Kobayashi, 2023). This experiment result could mean that microbiota of patients with endometriosis can contribute to disease progression (table 6). However, we still need more data of FTM being used as a treatment line of endometriosis.

Table 6. Microbiome and Nutritional Therapies for Endometriosis

Approach	Mechanism / Agent	Benefits	Limitations / Notes
Probiotics (L. gasseri)	Activates NK cells; modifies gut microbiota	Pain relief; suppresses lesion growth in mice	Human studies ongoing
Omega-3 PUFAs / ALA	Anti-inflammatory; microbiota modulation	Reduces lesion size, inflammation, PGE2; improves gut flora	Mostly preclinical data
FMT	Transplantation of healthy microbiota	Potential to reset dysbiotic gut environment	Experimental; no human trials yet

Gene and Cell-Based Therapies

Endometriosis is considered a complex disease characterized by widespread epigenetic and genetic defects, which makes gene therapy promising strategy of treatment (Zhao et al., 2012). Research has identified microRNA expression that is lower in patients with endometriosis. In mouse models, treatment with Let-7b, which is a specific microRNA, reduced endometroid lesions which could be a sign of its therapeutic potential. The inflammatory marker IL-6 was suppressed in the treated group, proving that Let-7b reduces inflammation associated with the disease (Sahin et al., 2018).

Moreover, endometriosis is an angiogenesis-dependent disease, meaning newly formed blood vessels are necessary for the survival and growth of lesions. Pigment epithelium-derived factor (PEDF) is a protein that inhibits angiogenesis (Zhao et al., 2012). In a study conducted by Zhao et al., (2012) intravenously administered PEDF was successfully distributed to endometriotic lesions in a rat model of peritoneal endometriosis and significantly reduced their size.

Cell-based therapy is an approach that is gaining attention as a potential future treatment for endometriosis. One of the cell therapy treatments that deserves particular attention is the use of adipose tissue-derived stem cells (ASCs). Administration of ASCs reduced stromal fibrosis and the proliferation of endometriotic epithelial cells in the endometrial tissues (Table 7). Moreover, ASC

administration decreased the expression of pro-inflammatory cytokines such as Mcp, IL-6, and Lif, as well as the pro-fibrotic cytokine tumor growth factor-β1 (Tgfb1) (Hirakawa et al., 2022).

Table 7. Gene and Cell-Based Therapies for Endometriosis

Therapy	Mechanism	Benefits	Limitations / Notes
Let-7b microRNA	Downregulates ERs, KRAS, IL-6	Reduces lesion size and inflammation	Preclinical; delivery systems still under development
PEDF (anti-angiogenic protein)	Inhibits new blood vessel growth in lesions	Reduces lesion size in animal models	Requires clinical translation
ASCs (stem cells)	Anti-fibrotic, anti-inflammatory; reduces cytokines like IL-6 and TGF-β1	Inhibits lesion progression; restores tissue balance	Experimental; long-term effects unknown

Surgery

Robotic-assisted laparoscopic surgery has gained increasing attention and is being adopted more frequently for endometriosis surgery. Robotic technology provides features like 3D vision, improved ergonomics, and reduced tremor effects (Ferrari et al., 2024; Lee & Kim, 2024; Ong et al., 2024). Robotic assistance may also be particularly helpful in increasing dissection precision and improving autonomic nerve identification and preservation, potentially resulting in better functional outcomes (Ferrari et al., 2024).

Despite promising possibilities of Robotic-Assisted Laparoscopic Surgery, studies comparing both minimally invasive surgical techniques show mixed results (Ferrari et al., 2024; Ong et al., 2024; Song et al., 2023). Published reports indicate that laparoscopic surgery characterizes a statistically significant lower operation and hospitalization time compared with the robotic technique. However, for bowel-deep infiltrating endometriosis, some studies strongly suggest that robotic surgery is not a better option. This technique was associated with longer operating time, but shorter hospital stays and fewer complications compared to the laparoscopic surgery (Ong et al., 2024). On the other hand, no significant differences were observed between the two techniques in terms of blood loss, rehospitalization rates, intraoperative and postoperative complications, or conversion rates (Song et al., 2023).

4. CONCLUSION

Endometriosis is a chronic and weakening condition that severely impacts patients' quality of life and requires a complex treatment approach. Managing endometriosis remains a challenge due to the variety of symptoms, disease progression, and patient responses to treatments. Traditional treatment strategies, such as NSAIDs, hormonal therapy, and laparoscopic surgery, remain a foundation of care. NSAIDs, while used the most commonly, have limited clinical relevance for managing endometriosis-related pain across studies. The inconsistent effectiveness data underscore the need for more rigorous research in this area. Hormonal therapies, particularly progestins and combined oral contraceptives, are the foundation for symptom control. At the same time, they seem beneficial in reducing lesion proliferation. However, side effect associated with their use, especially the androgenic effects and impact on bone density, proves the need for developing other treatment options with better tolerability. The GnRH agonists and antagonists at first seemed like ideal hormonal therapy options, providing hypoestrogenism. Unfortunately, they are associated with menopausal-like symptoms and bone loss. These side effect prevents clinicians from using GnRH agonist and antagonist as a long-term treatment option. Newer oral GnRH antagonists like relugolix and linzagolix have the ability to keep the estradiol levels within a therapeutic window. Their development represents the best of both worlds - combining effectiveness and safety for long-term use.

Surgical intervention, particularly minimally invasive laparoscopy, are a foundation of endometriosis treatment. They are mostly beneficial for women with significant organ involvement. Laparoscopy offers quicker recovery and better fertility outcomes, but on the other hand, it might need more specialized surgical training as it is more technically challenging. The integration of robotic-assisted laparoscopic surgery offers promising improvements in precision and ergonomics. However, long-term safety data is limited, and further research is necessary to assess the risk profile over an extended period of use.

Novel immunomodulatory therapies targeting the CD47-SIRPa signaling pathway and NK cells are gaining attention. This treatment approach could complement already existing hormonal strategies. Moreover, the role of microbiome, dietary interventions and supplementation are becoming essential strategies for controlling chronic pain and inflammation associated with endometriosis. It

starts a new wave of holistic approach to endometriosis management; however, future high-quality RCTs with long follow-up periods and standardized supplements formulations are needed to provide more substantial evidence. Modern pain management techniques, such as sacral neuromodulation and transcranial direct current stimulation, provide alternative options for patients with chronic pelvic pain. The success in pain relief of these approaches highlights the complex nature of endometriosis-related pain. Novel approaches, including gene and cell-based therapies, represent a promising but still experimental area. Evidence from several studies strongly suggests that technologies such as microRNA manipulation and adipose tissue-derived stem cells (ASCs) may hold promise for future endometriosis management, focusing on targeted treatments. Future research is needed to understand long-term outcomes better and integrate these strategies into clinical practice.

Endometriosis remains a challenging condition that requires a complex treatment approach. The shift from traditional to modern and experimental therapies shows a significant shift towards more personalized care. We can see the need for new strategies that address both symptoms and pathophysiology of endometriosis. Looking forward, future research should focus on large-scale, long-term clinical trials to validate these new therapies and explore the approaches that integrate pharmacological, surgical, and lifestyle interventions. A greater emphasis on patient-specific characteristics, including hormonal sensitivity, immune profile, and genetic background, may also help provide tailored strategies for managing endometriosis. Ultimately, the goal is to change from symptom management toward long-term disease modification and improved quality of life for all patients affected by endometriosis.

Author's Contributions

Paulina Wasilewska contributed to the study design, coordinated the writing process, and led the development of the final manuscript.
Olga Wojtczak was responsible for background research, clinical content input and refinement of the discussion section.
Kacper Zagaja supported data interpretation, helped organize the structure of the paper, and reviewed the final draft for consistency.
Justyna Wróblewska performed the initial literature screening, contributed to the introduction and conclusion sections.
Hubert Ziembicki assisted with referencing and table preparations.
Natalia Skrzypska assisted in literature analysis, handled formatting and technical editing and ensured adherence to submission guidelines.

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Informed consent

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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