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## The Role of Physical Activity in Reducing Endometriosis Pain

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#### Abstract

Endometriosis is a chronic condition characterized by the presence of endometrial tissue outside the uterine cavity. This leads to pain, inflammatory states, and disruptions in the functioning of pelvic organs, including infertility. Physical activity influences the symptoms of endometriosis associated with the presence of ectopic endometrial tissue in the body.

This study analyzes available scientific evidence regarding the role of physical activity in alleviating pain caused by endometriosis. Research findings indicate that regular physical exercise of varying intensity can provide benefits by reducing inflammation, improving pelvic blood flow, and reducing muscle tension. The impact of physical activity on the hormonal system, including the modulation of endorphin levels and the endocannabinoid system, may contribute to pain relief. The effectiveness of exercise in endometriosis therapy depends on the type of exertion, its intensity and frequency, as well as individual factors such as the severity of the disease and the patient's health status. Studies point to yoga, Pilates, and aerobic exercises as the most beneficial forms of activity. Regardless of the type of activity studied, the most crucial factor is the frequency and duration of the exercise. The study also emphasizes the need for further research to develop personalized recommendations for physical activity for patients with endometriosis.

In conclusion, physical activity can provide valuable support in the treatment of endometriosis, contributing to an improvement in the quality of life of patients through pain reduction and overall well-being.

### Keywords

endometriosis, endometriosis and lifestyle, endometriosis and physical activity

Endometriosis is a chronic condition characterized by the presence of endometrial tissue outside the uterine cavity. This leads to pain, inflammatory states, and disruptions in the functioning of pelvic organs, including infertility. Physical activity influences the symptoms of endometriosis associated with the presence of ectopic endometrial tissue in the body.

This study analyzes available scientific evidence regarding the role of physical activity in alleviating pain caused by endometriosis. Research findings indicate that regular physical exercise of varying intensity can provide benefits by reducing inflammation, improving pelvic blood flow, and reducing muscle tension. The impact of physical activity on the hormonal system, including the modulation of endorphin levels and the endocannabinoid system, may contribute to pain relief. The effectiveness of exercise in endometriosis therapy depends on the type of exertion, its intensity and frequency, as well as individual factors such as the severity of the disease and the patient's health status. Studies point to yoga, Pilates, and aerobic exercises as the most beneficial forms of activity. Regardless of the type of activity studied, the most crucial factor is the frequency and duration of the exercise. The study also emphasizes the need for further research to develop personalized recommendations for physical activity for patients with endometriosis.

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# **INTRODUCTION - What is Endometriosis?**

Endometriosis is a benign gynecological condition in which ectopic endometrial cells lining the uterus are found outside the uterine cavity. This condition affects up to 10% of women of reproductive age, with up to 70% experiencing symptoms. The main clinical symptom of endometriosis is severe pain during menstruation. Often, this is accompanied by dyspareunia, or pain during sexual intercourse, as well as chronic pelvic pain syndrome. Other conditions associated with endometriosis include irritable bowel syndrome, painful bladder syndrome, abdominal pain, migraine, reduced quality of life, and fatigue. It is suspected that all these ailments are rooted in the inflammatory and immunological pathways of endometriosis. Diagnosing endometriosis takes an average of 8 years, during which secondary musculoskeletal disorders and psychological disorders may develop.

### Pathophysiology of Pain in Endometriosis

Pain in endometriosis is a complex process involving various pathophysiological mechanisms, including inflammatory processes, neuromodulation, and hormonal and structural changes. Factors contributing to the inflammatory process in endometriosis include:

## **Pro-inflammatory Cytokines**

Pro-inflammatory cytokines are released by ectopic endometrial tissues (endometriotic lesions). These include IL-1, IL-6, TNF- $\alpha$ , and chemokines, which attract macrophages and other immune cells to the sites of disease [1]. These mediators enhance inflammatory processes and increase the sensitivity of nociceptors, leading to hyperalgesia [1].

## **Neoangiogenesis and Neurogenesis**

Endometrial lesions are highly vascularized due to the secretion of vascular endothelial growth factor (VEGF) by endometrial cells. VEGF is the primary factor regulating both pathological and physiological angiogenesis, including the cyclical angiogenesis that occurs during the menstrual cycle in the endometrial lining. VEGF, by binding to specific receptors on the surface of endothelial cells, transitions them from a resting state to an angiogenic phenotype, leading to proliferation, migration, and the formation of vascular cords. This results in abundant vascularization of endometrial tissue outside the uterine cavity [2]. Newly formed blood vessels not only supply nutrients to the lesions but also facilitate the growth of ectopic tissues, exacerbate inflammation, and intensify pain [2].

Endometriosis also promotes the growth and transformation of peripheral nerves within the lesions. This is likely due to the secretion of nerve growth factor (NGF) and NG-3 by ectopic endometrial tissue. This leads to dense innervation of endometrial lesions and the growth of new neurons, increasing nociceptor activity and pain perception [3], which intensifies with

each menstrual cycle. Newly formed nerves are often atypical and easily excitable, further contributing to pain.

### **Hormonal Dependence of Endometriosis**

The proliferation of endometrial tissue depends on estrogens. These hormones not only stimulate the growth of ectopic endometrial tissues [4] but also enhance the expression of pain mediators and receptors within the lesions, such as TRPV1 (vanilloid receptor). This leads to increased sensitivity to pain stimuli [4]. The chronic inflammatory process and activation of fibroblasts promote the formation of fibrous tissue and adhesions [5]. Endometrial lesions are often surrounded by fibrous scars that can compress nerves and blood vessels, increasing pain perception and leading to tissue remodeling.

# **Changes in the Central Nervous System**

Endometriosis can lead to changes in the spinal cord and brain, such as central sensitization, which maintains pain even after the lesions are removed. This mechanism resembles processes observed in chronic neuropathic pain [6]. Ectopic lesions can affect surrounding organs, such as the bladder or intestines, leading to pain associated with their function, such as painful urination or defecation [7].

## **Genetic and Epigenetic Studies**

Studies indicate the presence of altered gene expression in endometriosis. Mutations in genes related to the immune system, angiogenesis, and neurogenesis may contribute to the development of pain. Additionally, epigenetic changes, such as DNA methylation and histone modification, can influence the expression of genes related to pain perception [8].

### Dysmenorrhea

Dysmenorrhea is one of the most common symptoms of endometriosis. This pain is associated with menstruation and can be very intense, often requiring pharmacological treatment. It is caused by inflammation and the stimulation of pain receptors by inflammatory mediators, such as prostaglandins [9]. Prostaglandins cause uterine contractions, which can intensify pain perception [10].

# **Chronic Pelvic Pain**

Chronic pelvic pain is pain that lasts for at least six months and is not directly related to menstruation. It can be continuous or intermittent, often described as dull or burning. It may result from central sensitization, where the central nervous system becomes hypersensitive to pain stimuli [11]. Additionally, local inflammation and scarring can contribute to the exacerbation of this type of pain [12].

## Dyspareunia

Dyspareunia is pain that occurs during or after sexual intercourse. The main cause of dyspareunia is the local inflammatory process, the presence of scars and adhesions between pelvic organs. Dyspareunia can also be caused by mechanical irritation of endometriotic lesions during intercourse, leading to the stimulation of pain receptors [13]. Additionally, psychological factors such as stress and fear of pain can exacerbate this symptom [14].

## **Pain During Urination**

Pain during urination can result from direct pressure on the bladder by endometriotic lesions or scars. Mechanical pressure on the bladder by endometriotic lesions or scars can lead to the stimulation of pain receptors in this area [15]. Additionally, inflammation can cause hyperactivity of the bladder [16].

# **Pain During Defecation**

Endometrial adhesions and lesions present on the intestines can disrupt intestinal functions through mechanical pressure, leading to the stimulation of pain receptors in this area [17]. Additionally, the inflammatory state can cause hyperactivity of the intestines [18].

# **Referred Pain**

Referred pain is felt in a location different from the source of the pain. Referred pain can result from the stimulation of nerves that transmit pain stimuli from the pelvis to other parts of the body [19]. In endometriosis, pain can be felt in the back, legs, or buttocks. Additionally, central sensitization can contribute to this type of pain [20].

## **Neuropathic Pain**

Neuropathic pain is pain resulting from damage or dysfunction of nerves. In endometriosis, it can be caused by direct damage to nerves by endometriotic lesions or scars [21]. Additionally, inflammatory mediators can affect neuroplasticity, leading to chronic pain [22].

### How Physical Activity Affects Pain Perception

Physical activity influences estrogen levels by modulating the hypothalamic-pituitary-gonadal axis. Intense physical exertion increases the metabolism of estrogens in the liver, leading to their faster excretion and lower blood concentrations. Reducing estrogen levels limits the proliferation of endometrial lesions, thereby reducing inflammatory processes. Furthermore, exercise lowers leptin levels and improves insulin sensitivity, which reduces excessive estrogen production in adipose tissue [23,24].

## **Improvement of Hormonal Balance in Women**

Regular exercise supports hormonal balance by stabilizing the ratio of estrogens to progesterone. It reduces the activity of aromatase, an enzyme responsible for converting androgens to estrogens, which is particularly important in reducing pathological estrogenic effects [25,26].

### Impact of Physical Activity on the Immune System and Inflammatory Processes

### **Reduction of Pro-inflammatory Cytokines (IL-6, TNF-α)**

Moderate-intensity exercise lowers the levels of pro-inflammatory cytokines, such as IL-6 and TNF- $\alpha$ , by increasing the production of myokines (IL-10) by muscles. These myokines act as anti-inflammatory agents, inhibiting the production of cytokines associated with chronic inflammatory states [27,28].

### **Improvement of Macrophage Function and Reduction of Local Inflammation**

Physical activity promotes the transformation of pro-inflammatory M1 macrophages into antiinflammatory M2 macrophages, leading to a reduction in local inflammation in endometrial lesions. Additionally, exercise improves oxidative-antioxidative balance, reducing tissue damage and limiting the release of inflammatory mediators [29,30].

### **Neurophysiological Mechanisms of Pain Reduction**

## Stimulation of Endorphins and Other Pain-Counteracting Neurotransmitters

Exercise stimulates the release of  $\beta$ -endorphins, which act as natural opioids, blocking pain receptors in the nervous system. Beta-endorphins bind to two subtypes of opioid receptors present in the peripheral nerve endings, central primary afferent neurons, dorsal root ganglia, and peripheral sensory nerve fibers. This process activates the internal pain-relief system, leading to the release of GABA and a decrease in substance P levels, which inhibits the transmission of pain signals. Additionally, increased levels of serotonin and dopamine play a crucial role in reducing pain perception and improving mood [31].

#### **Reduction of Central Sensitization of the Nervous System**

Regular physical activity decreases central sensitization to pain stimuli by reducing the activity of neurons in the dorsal horns of the spinal cord. Furthermore, it supports neuroplasticity, which limits the chronic perception of pain in endometriosis [32].

### **Reduction of Stress and Depression as Factors Intensifying Pain Perception**

Physical activity lowers cortisol levels by regulating the hypothalamic-pituitary-adrenal (HPA) axis. It also increases the production of serotonin and dopamine [33], counteracting depression and anxiety, which can intensify the subjective experience of pain. Reducing stress and improving mood is particularly important as it translates to a better quality of life for patients with endometriosis.

Clinical and observational studies confirm that physical activity can effectively reduce pain associated with endometriosis, influencing both hormonal and immunological mechanisms.

One study from 2021 showed that women participating in a 12-week yoga program reported a reduction in pelvic pain by approximately 25% compared to the control group, which did not practice such activity [35]. Analyses indicate that regular physical activity (a minimum of 150 minutes per week) is associated with pain reduction and improved quality of life. In a 2019 study involving over 800 women, it was observed that moderate-intensity exercise reduced the frequency and intensity of painful episodes [34,36].

# Analysis of Types of Physical Activity

### Yoga

Yoga positively influences pain by improving flexibility, regulating breathing, and reducing stress levels. One study found that regular yoga practice lowers cortisol levels and increases endorphin production, directly reducing pain perception [36,37].

## **Aerobic Training**

Aerobic exercises, such as running or cycling, improve blood circulation and reduce inflammatory states by decreasing pro-inflammatory cytokines (e.g., TNF- $\alpha$ ). Studies show that regular aerobic training of moderate intensity for 30 minutes a day, 5 days a week, leads to a 15-20% reduction in pain [38].

### **Strength Training**

Strength exercises strengthen the pelvic floor muscles, reduce muscle tension, and improve stability in the pelvic area. A 2020 study demonstrated that an 8-week strength training

program improved both the quality of life and reduced pain perception in patients with endometriosis [39].

### Intensity and Frequency of Exercise vs. Therapeutic Effectiveness

## **Moderate Intensity**

Regular physical activity of moderate intensity (walking, yoga) is well-tolerated by most patients and effective in reducing pain [36,37].

# **High Intensity**

High-intensity exercise also reduces inflammation and improves immune system conditioning, but its use requires caution depending on the stage of the disease [38,39].

## Frequency

Exercises performed at least 3-4 times a week for at least 30 minutes provide the greatest therapeutic benefits.

## **Endocannabinoids and Pain Reduction in Endometriosis**

Endogenous cannabinoids play a crucial role in pain regulation, especially in chronic conditions like endometriosis. The endocannabinoid system (ECS) includes CB1 and CB2 receptors, endogenous ligands (e.g., anandamide and 2-arachidonoylglycerol), and enzymes involved in the synthesis and degradation of these ligands. The ECS influences the nervous system and inflammatory processes, making it essential for pain reduction [41].

## **CB1 Receptors**

CB1 receptors are present in the central and peripheral nervous systems, where their activation leads to the inhibition of pain neurotransmitter release.

## **CB2** Receptors

CB2 receptors, mainly found on immune cells, reduce inflammatory processes, which can be particularly important in endometriosis, where chronic inflammation plays a key role in pathophysiology [42].

## **Dysregulation of ECS in Endometriosis**

Studies have shown lowered levels of anandamide in endometrial tissues of patients with endometriosis. This can lead to increased pain perception and exacerbated inflammatory states.

#### Impact on Uterine Contractions

Endocannabinoids regulate the activity of smooth muscles, including the uterus. Their deficiency can lead to intensified contractions, exacerbating pain [43].

#### Impact of Physical Activity on Endocannabinoid Release

Physical activity can significantly increase the levels of endogenous cannabinoids, contributing to pain reduction.

### **Increased Anandamide (AEA) Levels**

Aerobic exercises of moderate or high intensity lead to an increase in anandamide levels, activating CB1 and CB2 receptors [42], which reduces pain perception and inflammation. A 2020 study observed that runners had significantly higher AEA levels post-exercise, correlating with pain reduction [43].

# **Reduction of Inflammatory State**

Activation of CB2 receptors by endocannabinoids decreases the levels of pro-inflammatory cytokines (e.g., TNF- $\alpha$ , IL-6), reducing local inflammation in endometrial lesions [43,44].

### **Improvement of Mood and Pain Perception**

Physical activity stimulates the release of endocannabinoids and other neuromodulators, such as endorphins, which synergistically contribute to pain reduction and improved psychological well-being [45,46].

# Limitations and Controversies in Research Findings

# Lack of Standardization in Methodology

Different research approaches (duration of interventions, types of activities) make it difficult to compare results [38].

# **Individual Differences**

Women with advanced endometriosis may have difficulty tolerating certain forms of exercise, limiting their use as a universal therapy. Additionally, each individual has different predispositions to specific types of physical exertion [38,39].

# Lack of Long-Term Studies

Most studies focus on the short-term effects of physical activity. Further research is needed to assess its impact on long-term disease progression and chronic pain [39,40].

## Conclusion

Nevertheless, all available studies to date indicate a positive impact of physical activity in the therapy of endometriosis. Regular exercise, whether it be yoga, aerobic training, or strength training, has been shown to reduce pain, improve mood, and enhance the overall quality of life for patients. The benefits of physical activity extend beyond immediate pain relief, influencing both hormonal and immunological mechanisms that are crucial in managing the symptoms of endometriosis.

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