

IMPACT OF PHYSICAL ACTIVITY AS AN AID TO DRUG TREATMENT FOR ENDOMETRIOSIS

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Abstract: Background: Endometriosis is a disease in which its diagnosis is often late, and the pharmacology used sometimes does not match the stage of the disease; in addition, it has limitations regarding effectiveness in several cases. **Interpretation of this article in the current context:** In the database of this research in the references analyzed, it was noticed that in sedentary women, the symptoms may be more aggravated compared to non-sedentary women. **New knowledge added by this research:** The practice of physical exercise associated with drug treatment can have a considerable improvement in the symptoms of Endometriosis and, consequently, bring benefits to the quality of life of women with this disease, in addition to lower consumption of medication and avoiding polypharmacy in these cases **Implications for clinical practice after this study:** It is suggested that more studies be carried out to verify the influence on different stages of Endometriosis and the impact of the benefits of physical activity in these conditions.

Keywords: Endometriosis; Physical activity; Pharmacological Treatment;

INTRODUCTION

Endometriosis is a disease characterized by endometrial tissue in locations outside the uterus. The incidence of Endometriosis varies from 2 to 15% in women of reproductive age. Among infertile women, the incidence reaches 20-50%. Clinical manifestations include dysmenorrhea, chronic pelvic pain, dyspareunia and infertility. In most cases, diagnosis occurs late after the appearance of symptoms (Della Corte *et al.*, 2020).

For some time now, research has sought to evaluate the impact of physical exercise – in a supplementary way – as an ally in improving the quality of life of these patients ((Hansen *et al.*, 2021)). This condition raises the guiding question of this study: *what are the*

characteristics of women with Endometriosis who perform physical activity – in terms of medication use – compared to those who are sedentary?

This study then aimed to progress in resolving this issue. From this, one could think about developing programs to encourage physical activity for these patients and protocols to help health professionals identify this ally in treatment. Furthermore, the desire is to disseminate the understanding that treating this multifactorial disease goes beyond the purely medicinal aspect.

METHODOLOGY

This observational study was carried out through an *online survey* among women diagnosed with Endometriosis and participants in the “Endometriosis Uncensored” group on a given social network. This community has around 59 thousand women and has the presence of health professionals to moderate the group. The questionnaire was applied via the Google Forms[®] platform from May to June 2021. The research was developed with the consent and agreement of the moderators of the group above, who presented the research to community members and invited group participants.

As it involves human beings, the legislation in force in Brazil was respected, and the present project was submitted to the Research Ethics Committee (CEP) of UNIVILLE, being assessed and evaluated as approved, obtaining an approval protocol with CAAE registration 26897619.2.0000.5366.

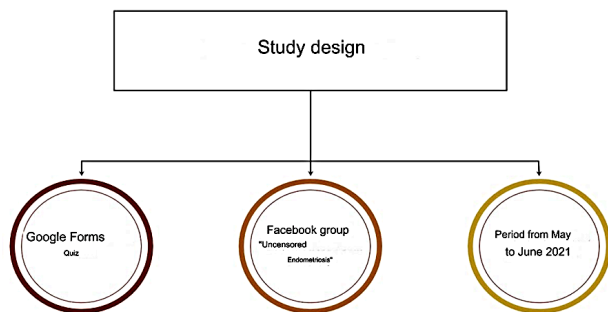


Figure 1: Study design. Source: from the authors.

The studied population was made up of women who reported having been diagnosed with Endometriosis, counting from the date of the first disabling pain. The “physical activity” group included all those who mentioned whether or not they performed physical activity, considered here aerobic and anaerobic activities performed at least once or twice a week. Outside this criterion, they were considered to be in the “sedentary” group. The data collected referred to medications consumed, listed below:

- NSAIDs [nonsteroidal anti-inflammatory drugs]
- CHO [hormonal contraceptives]
- NSAIDs associated with CHO [hormonal contraceptives]
- Dienogest,
- Progesterone IUD,
- Danazol,
- Goserelin,

Women who did not agree to participate or completed the questionnaire incompletely were excluded from the research.

Quanto à amostragem, considerou-se dados da literatura nacional recente, sobre a prevalência de mulheres com endometriose no Brasil, e por meio da ferramenta de cálculo amostral on-line, Converter®, estabeleceu-se o valor mínimo de 341 mulheres para o estudo em questão.

RESULTS

Figure 2 shows the results of the screening carried out and the age group.

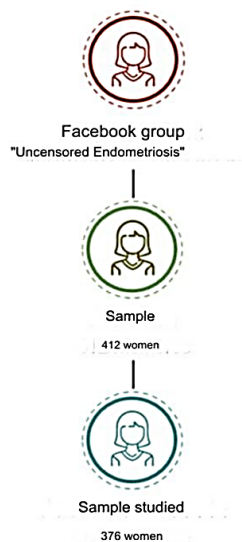


Figure 2: Population screening results. Source: from the authors.

The studied sample consisted of 376 patients with Endometriosis. Regarding the characterization according to age group, the majority (38.56%) are between 35 and 40 years old, followed by those between 31 and 34 years old (19.25%), those between 25 and 30 years old (18.88%), those over 41 years old (15.15%) and finally, those between 18 and 24 years old (7.45%).

About menarche, the majority had it at the age of 12 (23.40%), similar to the numbers of menarche at 11 (23.40%) and 13 (22.61%). There was a more significant discrepancy in menarche after more than 14 years (15.96%) and those who had it less than ten years (11.97%). Regarding the stages of Endometriosis, 20 patients reported being in stage I (5.32%), 167 patients in stage II (44.41%), 46 patients in stage III (12.23%) and 143 patients in stage IV (38.03%).

Most patients had been diagnosed for over six years (55.85%). Below this, the numbers for the different diagnosis times were very

close. Most of the patients had not undergone a hysterectomy (88.82%).

PHYSICAL ACTIVITY VERSUS SEDENTARY LIFESTYLE: IMPACT ON THE AMOUNT OF MEDICATION USED BY THE GROUPS

Among the sedentary: 43 (22.87%) use NSAIDs, 42 (22.87%) use continuous combined CHO, 32 (17.01%) use NSAIDs combined with continuous CHO, 14 (7.44%) use dienogest, 10 (5.31%) use progesterone IUD, 2 (1.06%) use danazol, 24 (12.76%) use goserelin, 4 (2.12%) bioidentical progesterone, 1 (0.53%) resveratrol and 14 (7.44%) no medication.

Among those who do physical activity at least once a week: 44 (26.03%) use NSAIDs, 1 (0.59%) anastrozole, 32 (18.93%) continuous combined CHO, 18 (10.65%) NSAIDs coupled with continuous combined CHO, 11 (6.50%) dienogest, 17 (10.05%) progesterone IUD, 22 (13.01%) goserelin, 1 (0.59%) naltrexone, 1 (0.59%) estrogen, 1 (0.59%) gestrinone implant, 2 (1.18%) bioidentical progesterone, 1 (0.59%) resveratrol and 18 (10.65%) no medication.

Among those who do physical activity at least 2 to 3 times a week: 8 (42.10%) use NSAIDs, 4 (21.05%) continuous combined CHO, 1 (5.26%) NSAID associated with continuous combined CHO, 1 (5.26%) progesterone IUD, 1 (5.26%) goserelin, 4 (21.05%) no medication.

DISCUSSION

The discussion will follow the scheme shown in Figure 3, ranging from the macro context to the conclusion of this work.

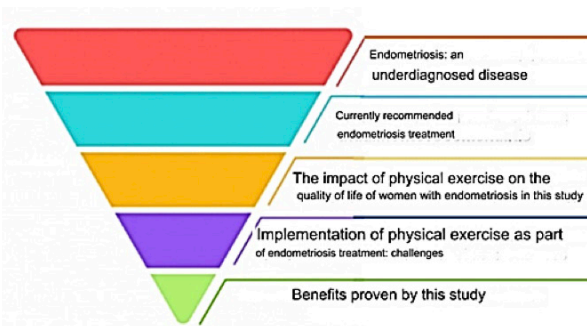


Figure 3: Discussion scheme. Source: from the authors.

ENDOMETRIOSIS: AN UNDERDIAGNOSED DISEASE

Endometriosis is a clinical and recurrent condition characterized by functional endometrial tissue outside the uterine cavity and myometrium (Rosa & Silva et al., 2021). The disease can be divided into three types: peritoneal, ovarian and deep. Peritoneal is characterized by the presence of superficial implants in the peritoneum; ovarian, through superficial implants in the ovary or cysts; and deep is defined as a lesion that penetrates the retroperitoneal space or the wall of the pelvic organs, with a depth of 5 mm or more (Podgaec et al., 2018).

Based on the age range of the patients studied, these numbers are in line with the persistence of a late diagnosis of Endometriosis today. This is because its symptoms can be confused with those of other illnesses, such as pelvic infections, uterine myomatosis, and urological and gastrointestinal disorders (Thiel et al, 2024)

In the study carried out by Cardoso et al, (2020), which evaluated the epidemiological and clinical profile of women with Endometriosis treated in two reference hospitals in Rio de Janeiro, it was found that the majority of

women (111) were aged between 30 and 39, corresponding to 46.8%. Regarding age at menarche, an average of 12.5 ± 1.7 years was observed, with 43.5% of patients reaching menarche between 12 and 13 years.

Delays in diagnosis consequently lead to late initiation of treatment, just as a lack of knowledge about the disease can lead to inadequate treatment. This affects patients' quality of life, increasing healthcare costs, causing hospitalizations, consultations or exams, intimate interpersonal problems, risk of spreading lesions to other organs and infertility (Trindade et al., 2021; Tennfjord et al, 2021).

CURRENTLY RECOMMENDED ENDOMETRIOSIS TREATMENT

Current treatment for Endometriosis consists mainly of nonsteroidal anti-inflammatory drugs (NSAIDs), hormonal contraceptives, gonadotropin-releasing hormone (GnRH) analogs, and aromatase inhibitors. There is not enough data to determine a gold standard treatment, so choosing the best treatment involves shared decision-making with the patient and is based on the severity of symptoms, patient preferences, medication side effects, treatment effectiveness, needs, costs and availability of contraceptives (De-Wert et al, 2019).

For patients with mild to moderate pain, the first line is the combination of NSAIDs and hormonal contraceptives due to the low risk and fewer side effects. Similar data were found in the present study since the most used medications are NSAIDs, used by 25.53% of patients. Continuous combined oral hormonal contraceptives (CHO) come in second place, with 21.01% of women using them and 9.57% of patients not using any medication (De-Wert et al, 2019).

GnRH analogs are used with additional hormonal therapy or aromatase inhibitors

(Mardon et al, 2023a). In the results obtained, 15.4% of women were using some GnRH analog with additional hormonal therapy, and 0.53% were using aromatase inhibitors (Mardon et al, 2023a).

In the present study, 11.17% of patients opted for hysterectomy - a surgical approach. A laparoscopy is performed to determine the diagnosis and then treatment, which can be carried out conservatively (maintains the uterus and ovarian tissue) or definitively - removal of the uterus and ovaries (De Wert et al, 2019). Surgical intervention is the definitive treatment for Endometriosis. However, this procedure is not without risks and is associated with the recurrence of pain (Mardon et al, 2023b). In patients with Endometriosis in stages I and II, performing excision of the foci is recommended, not just diagnostic laparoscopy. As for patients with stages III and IV, there has yet to be a consensus on whether a surgical approach is indicated only for the treatment of infertility (Thiel et al 2024). Today, the treatment of Endometriosis is focused on pharmacology and the possibility of surgery.

Laparoscopy was the most used diagnostic method, and the majority of patients with a surgical diagnosis had stage III/IV endometriosis, according to data found in the study carried out by Cardoso et al. (2020).

THE IMPACT OF PHYSICAL EXERCISE ON THE QUALITY OF LIFE OF WOMEN WITH ENDOMETRIOSIS

Endometriosis is associated with significant physical and emotional morbidity resulting from chronic pain, infertility, social isolation, economic impact and interference in emotional and family relationships. Due to the complex etiology of the disease, a portion of patients undergoing drug and surgical interventions do not experience satisfactory

remission of symptoms, remaining in pain, which, in general, contributes to a reduction in quality of life.

Therefore, physical exercise has been seen as an ally in maintaining quality of life and an auxiliary treatment for Endometriosis, possibly contributing to different aspects. Arslan et al (2024) reported a protective effect of physical exercises practiced early and with a frequency of at least two hours per week. The reduction in serum estradiol levels in women who practice aerobic exercise regularly is associated with the release of beta-endorphins, which would inhibit GnRH and, consequently, the hypothalamic-pituitary-ovarian axis, reducing the intensity of symptoms (Tennfjord et al, 2021).

Furthermore, evidence suggests that endometriosis-related symptoms result from a local peritoneal inflammatory process caused by ectopic endometrial implants. The protective factor of regular physical activity has been evaluated in treating inflammatory diseases, considering some studies that describe that physical activity would increase the systemic levels of several cytokines with anti-inflammatory properties (Hansen et al, 2021)

However, the scientific literature regarding the benefits of physical exercise for patients with Endometriosis needs to be more conclusive. Studies in the United States indicated that the systematic practice of physical exercise was associated with the absence of a few depressive or anxiety symptoms (Sevindir *et al.*, 2014).

Studies indicate that practicing physical activity for less than 150 minutes a week is the most significant indicator of a sedentary lifestyle (BRAZIL, 2002). Among the patients studied, 188 are sedentary, 169 perform physical activity at least once a week, and 19 perform physical activity 2 to 3 times a week. Therefore, 50% of the patients studied are sedentary, representing a very worrying

rate. A sedentary lifestyle is considered a global public health problem and is present in mortality and disability rates through its consequences. It presents risk factors such as high blood pressure, cardiovascular diseases, and some types of cancer, such as breast and colon cancer, among many other consequences (WHO, 2003).

Given the treatments used, the most commonly used medication is NSAIDs, whether by patients who exercise more frequently or those who are sedentary. This can be a problem because, according to Lefebvre et al, (2020), these medications can reduce blood flow to the kidneys, thus causing damage to renal tissue due to their inflammatory substances. Furthermore, they can cause swelling and fluid retention, increasing pressure (Lefebvre et al, 2020).

The medication that appears in second place in all classes is continuous combined oral contraceptives (CHO). It is interesting to note that there is an indirect relationship between the frequency of physical exercise and the associated use of NSAIDs with continuous combined CHO. As the frequency of exercise increases, the use of this combination of drugs decreases by 17.01% of those who are sedentary, 10.65% of those who exercise once a week, and 5.26% of those who exercise at least twice a week (Tennfjord et al, 2021).

Dienogest, bioidentical progesterone, and resveratrol appear only in sedentary people and those who exercise only once a week. The progesterone IUD appears in three classes, as does goserelin. Danazol appears only in sedentary people. Anastrozole, naltrexone, oestrogel and the gestrinone implant appear only in those who practice physical activity once a week (Thiel et al, 2024).

Furthermore, it can be seen that the percentage of women with Endometriosis who do not use any medication increases directly with the increase in the frequency

of physical exercise per week. Among those who are sedentary, 7.44% do not use any medication; among those who exercise at least once a week, 10.65% do not use any; and finally, among those who exercise at least 2 to 3 times a week, 21.05% do not use any medication (Thiel et al, 2024).

Despite this, it is not intended to state that the non-use of medication attests to the effectiveness of physical activity in treatment. The aim is to understand that physical activity, by reducing chronic pain and improving patients' psychological and social aspects, improves their quality of life to the point that it can make them less dependent on drugs (Thiel et al, 2024)

IMPLEMENTATION OF PHYSICAL EXERCISE AS PART OF ENDOMETRIOSIS TREATMENT

The practice of any bodily movement produced through energy expenditure, including activities performed during work, games, domestic tasks, traveling and leisure activities, has gradually increased in the population's routine. As a result, you can currently find gyms, parks, and numerous sports centers in cities that feature various activities. Choosing the appropriate practice depends on several factors, which can vary between group or individual activities, those that require specific equipment and infrastructure, and whether or not a vital investment is made, but in particular, whether they focus on individual tastes (Tennfjord et al, 2021).

Several studies highlight the benefits that exercise can bring to both physical and mental health, such as strengthening bones and muscles, reducing blood pressure, possible weight reduction, reducing blood pressure and helping to control blood sugar levels, in addition, stress management, learning a skill, teamwork, socialization, character building,

constructive use of time, improved decision-making and self-confidence are observed (Sevindir, et al, 2014). Before implementing physical activity into anyone's routine, it is recommended that examinations be carried out to assess the individual's general health status so that the doctor is aware of the physiology of exercise in women and their previous health history, taking into account the necessary care so that this practice does not become harmful.

Given this need for medical evaluation, it is understood that there is a need for monitoring by a trained professional during the activity, such as a gym teacher or physiotherapist. The beginning of the practice should be done slowly, especially for previously sedentary individuals, starting with lighter activities, such as short walks, that can evolve by increasing the frequency or duration of the exercise. Ideally, the practice should occur most days of the week, lasting between 30 and 90 minutes (Arslan et al, 2024).

Therefore, given the information presented, the hypothesis is confirmed that the practice of physical activities has a relevant impact on the health of the female population and should be implemented as an adjuvant in treating patients with Endometriosis. To this end, doctors must be trained during graduation to understand the limitations of the pathology, enabling the prescription of appropriate and individualized activities. Furthermore, the importance of encouraging the production of research in the area and disseminating the knowledge obtained is highlighted. Even in the face of limitations such as the small sample size, the data from the present study may be interesting for more extensive studies in the future and contribute to the health area as a whole (Pinto et al, 2023).

CONCLUSION

The purpose of this article, in addition to observing the impact of physical exercise on the treatment of Endometriosis, was to provide more information to health professionals to improve healthcare quality. It is also expected that the professional understands that treating this multifactorial disease goes beyond just pharmacological therapies and that it is essential to prescribe an individual therapeutic project for each patient, focusing on the singularities of each woman.

When carrying out this research, it was noticed that there needs to be more scientific literature that analyzes physical exercise and

medications in treating the disease. However, based on the references analyzed and the database of this research, it was noticed that the symptoms may be more aggravated in sedentary women than in non-sedentary women. Thus, it was concluded that the practice of physical exercise associated with drug treatment can significantly improve the symptoms of Endometriosis and, consequently, bring benefits to the quality of life of women with this disease.

Therefore, more statistical studies should be carried out to verify the magnitude of the influence of the variables and confirm this tendency to improve the quality of life of patients who practice physical exercise.

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