Krupa Adrianna, Padała Olga, Putowski Maciej, Konopelko Michał, Piasek Ewa. Available treatment methods for endometriosis. Journal of Education, Health and Sport. 2019;9(7):178-184. eISSN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.3269215
http://ojs.ukw.edu.pl/index.php/johs/article/view/7119
https://pbn.nauka.gov.pl/sedno-webapp/works/917440

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part B item 1223 (26/01/2017).
1223 Journal of Education, Health and Sport eISSN 2391-8306 7

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 20.06.2019. Revised: 25.06.2019. Accepted: 04.07.2019.

Available treatment methods for endometriosis

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KEY WORDS:
endometriosis, treatment, pelvic pain, infertility

ABSTRACT
Introduction and and purpose of paper:
The aim of this paper was to present modern methods of treatment for endometriosis.

Endometriosis is a chronic inflammatory condition of women that is characterized by the implementation of endometrial tissue outside the uterus. It affects 7 to 15% of menstruating women, and 35 to 50% of women treated for infertility.
State of knowledge:
Diagnosis of endometriosis is made on the basis of well-collected gynecological history, clinical examinations and imaging techniques. The golden standard for diagnostics is laparoscopy with subsequent histological examination of the material collected during the procedure. Among the methods of treatment in women with endometriosis, pharmacological and surgical treatment is applied. The pharmacological agents most commonly used in endometriosis are: combined hormonal contraceptives, progestins and anti-progestins, GnRH agonists and antagonists, aromatase inhibitors, Danazol and non-steroidal anti-inflammatory drugs (NSAIDs). Pharmacological treatment is only symptomatic, not cytoreductive, therefore, to remove endometriosis lesions, surgery should be performed. There are two ways to perform surgery: laparotomy and laparoscopy. Surgical treatment of endometriosis may be associated with local excision of lesions and sometimes even removal of the entire organ. Treatment should be conducted in consultation with the patient and her wishes. Conservative treatment is most commonly used among women of reproductive age.
Summary:
The pharmaceutical or surgical treatment require an individual approach and deliberated informed consent of patient. Pharmacological treatment is only symptomatic, not cytoreductive, therefore, to remove endometriosis lesions, surgery should be performed.

INTRODUCTION

Endometriosis is a chronic inflammatory condition of women that is characterized by the implementation of endometrial tissue outside the uterus. Ectopic endometrium has functional similarity to uterus endometrium which in consequences produces menstrual excretion in its implementation place. It affects 7 to 15% of menstruating women, and 35 to 50% of women treated for infertility. There are three types of endometriosis: peritoneal, ovarian and deep infiltrating endometriosis. The most common symptoms, which allow it to suspect endometriosis are dyspareunia, dysmenorrhoea, pelvic pain syndrome and infertility. But not all patients are suffering from symptoms of this disease.
Etiology of endometriosis is still unclear and different hypothesis are used to explain causes. The most popular hypothesis are retrograde menstruation, alteration of the immune system, ectopic differentiation of mesenchymal stem cells, and genetic and environmental factors. [1,2]

PURPOSE OF THE PAPER

The aim of this paper is to present modern methods of treatment for endometriosis.

STATE OF KNOWLEDGE

DIAGNOSIS

Despite the dissemination of knowledge about endometriosis, still in many European countries, the diagnosis is delayed up to 10 years. [3] A well-established gynecological interview can significantly improve the chance of correct diagnosis. Another key issue is the physical examination of a patient suspected of endometriosis. During the clinical examination, the diagnosis may be indicated by a presence of induration or nodules of the rectovaginal wall, visible vaginal nodules in the posterior vaginal fornix or masses in adnexal

examination. Retroverted uterus and its small mobility are also common with this disease. Endometriosis can be suspected, even if the clinical examination shows no changes in the pelvic organs. Imaging techniques that can be helpful in diagnosing are ultrasound and MRI. However, the only reliable method (golden standard) to diagnose endometriosis is diagnostic and surgical laparoscopy with subsequent histological examination of the material collected during the procedure. [1,3]

AVAILABLE TREATMENT METHODS

Among the methods of treatment in women with endometriosis, pharmacological and surgical treatment is applied.

1. Pharmacological treatment

Pharmacological treatment aims to reduce endometriosis-associated pain, inhibit its further development and restore fertility. Through the empirical use of analgesics and hormones, one can achieve the abolition of nagging symptoms without the need for laparoscopic surgery. However, before introducing this therapy other causes of pelvic pain should be considered and excluded if possible. [1,3] Pharmacological therapy is often used as a complement to surgical treatment. It is used to reduce lesions before surgery and in the postoperative period. However, there is no evidence-based research to recommend systematic pre-operative hormonal therapy solely to prevent surgical complications or facilitate surgery. [4] The pharmacological agents most commonly used in endometriosis are: combined hormonal contraceptives, progestins and anti-progestins, GnRH agonists and antagonists, aromatase inhibitors, Danazol and non-steroidal anti-inflammatory drugs (NSAIDs).

1.1 Combined hormonal contraceptives (CHC)

Combined hormonal contraceptives are often used to treat the endometriosis-associated pain in form of dyspareunia, dysmenorrhoea or chronic pelvic pain. [5] This is usually an empiric first line treatment and it also improves the quality of life of women with endometriosis. Furthermore, their frequent use is associated with additional benefits, such as contraceptive protection, control of the menstrual cycle and long-term safety. [3] However, their use does not devoid side effects, which may include the increased risk of thromboembolism in some populations. [6] Although, in some observations of patients using CHC for the treatment of endometriosis-associated pain, there is a higher percentage of women still experiencing pain at the end of treatment compared with other hormonal agents. [7]

1.2 Progestins and anti-progestins

Progestins such as medroxyprogesterone acetate, dienogest, cyproterone acetate or norethisterone acetate and anti-progestins (gestrinone) are recommended in the treatment for endometriosis-associated pain. [8] They are usually used as the second line of treatment, continuously for a minimum of 6 months. Side effects of their use may be acyclic uterine bleeding, painful breast swelling and retention of body fluids. [1]

1.3 Gonadotropin-releasing hormone (GnRH) agonists

GnRH agonists such as nafarelin, leuprolide, buserelin, goserelin or triptorelin are second line of treatment for endometriosis-associated pain. [9] They have similar effectiveness in treating the pain as other drugs used in the therapy, but they have more side effects and contraindications. The most serious side effect of this drug may be reduce bone density and hypoestrogenic symptoms. Therefore, hormonal add-back therapy is recommended to prevent them. [10] As well as physical exercise and calcium supplementation. [1] When GnRH

agonist are compared with low dose oral contraceptives its showed that there are no difference in treating endometriosis-associated pain. [5] Which favors the use of contraceptives to avoid complications caused by GnRH.

1.4 Aromatase inhibitors

Aromatase inhibitors block synthesis of estrogens (from androgens) in ovaries, fat tissue and endometriosis lesions. Through their mode of action they lead to severe hypoestrogenism and related side effects such as: hot flashes, headaches, lowered libido, breast atrophy and high risk of reduced bone density. Therefore aromatase inhibitors are the last line of treatment, used only when other therapy methods have failed. [1]

1.5 Danazol

Danazol is a drug inhibiting the synthesis and release of gonadotropins, and ovarian hormone synthesis. The result of its use is inhibition of ovulation, absence or shortening of menstrual bleeding and endometrial atrophy. [11] However, due to numerous side effects such as weight gain, acne, seborrhea, hirsutism, atrophic vaginitis, hot flashes, decreased libido, virilism, voice alteration, negative effect on the lipid profile, it is nowaday rarely used. [2]

1.6 Non-steroidal anti-inflammatory drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs inhibit the synthesis of prostaglandins, thus contributing to the reduction of inflammation and relief of pain. Therefore, they are often used to treat the pain associated with endometriosis. Although, they should be used prudently considering the side effects of their frequent use, like inhibition of ovulation, risk of gastric ulceration and cardiovascular diseases. [2,3]

2. Surgical treatment

Pharmacological treatment is only symptomatic, not cytoreductive, therefore, to remove endometriosis lesions, surgery should be performed. The indications for the surgical treatment of endometriosis are pain in the pelvic area, infertility in the course of endometriosis, deep infiltrating endometriosis, and ovarian endometrial cysts. Surgical treatment of endometriosis may be associated with local excision of lesions and sometimes even removal of the entire ovary or uterus. The decision about the treatment should be made after consultation with the patient. Patient's reproductive plans must be taken under consideration as well as the extent of endometrial changes, and the severity of symptoms induced by endometriosis. Among young women of reproductive age, conservative treatment is the most common approach with a complete excision of the lesion with the preservation of genital organs and restoration of normal anatomy in the pelvis. However, such conservative therapy is associated with a high recurrence rate (13% after 3 years, 40% after 5 years), [1] which may oftenly need a radical solution, including excision of the organ. In the case of perimenopausal women, the treatment of severe endometriosis involves the removal of the uterus with adnexa. The result of this procedure is the induction of surgical menopause resulting from bilateral ovariectomy. [1,2]

Classical and laparoscopic surgery give similar results in the endometriosis-associated pain and have similar complications, including damage to the bladder and ureter. [1,3] However, due to less pain, shorter hospital stay and better cosmetic results, laparoscopy is the preferred method. [3] Laparoscopy with subsequent sampling for histological examination is also the only reliable method to diagnose endometriosis. However, if during its performance, the operator determines the presence of endometrial changes, he should remove them. To this end, their removal may be performed by their excision, electrocoagulation or vaporization by

laser. But not all of them are always suitable. During surgery for patients with ovarian endometrioma, cystectomy is the preferred option instead of drainage and coagulation, [12] and vaporization. [13] This is due to the advantage in the treatment of pain [12] and a smaller number of recurrences after the use of this type of procedure. [13]
In case of treatment of deep infiltrating endometriosis, complete excision of endometriosis should be performed. This may even involve the excision of parts from surrounding organs such as the sacro-cervical ligaments, the upper part of the posterior vaginal wall, part of the bladder wall or the bowel section. It is not recommended to cut out such advanced changes during diagnostic laparoscopy. It is necessary to finish the diagnosis in advance and obtain the patient's informed consent for such an extended procedure. [2]
Postoperative hormonal therapy is used to prevent recurrences. Especially in situations when resection of all the changes was not possible or when there are no certainty about the radicality of the procedure. [1]
In cases where conservative treatment did not work in chronic pain, procedures such as pre-cross neurectomy or uterine neurotransmission were performed. However, they are ineffective and can cause numerous complications such as constipation or prolapse of the uterus. [1,2]

3. Alternative methods and options for future

Complementary treatments, like acupuncture, exercise, electrotherapy, and yoga have been used to alleviate the symptoms of endometriosis. Only acupuncture has demonstrated a significant improvement in outcomes, however other approaches demonstrated positive trends toward improving symptoms. [14] There are data suggesting that melatonin may be useful as an adjunct to current endometriosis treatments. [15] Some studies indicate the roles of vitamin D in the development and progression of endometriosis. Vitamin D supplementation can relieve pain and improve endometrial receptivity associated with endometriosis and play a preventive and therapeutic role. [16] An important direction of research on the treatment of endometriosis may be a modification of microbiota. There are studies confirming altered bacterial composition in patients suffering from endometriosis compared to a healthy control group. [17]

SUMMARY

Endometriosis as a common affliction in women, occurs widely in the world population and should not be underestimate by the physicians. Endometriosis may lead to the dyspareunia, dysmenorrhoea, pelvic pain syndrome and infertility. The pharmaceutical or surgical treatment require an individual approach and deliberated informed consent of the patient. Pharmacological treatment is only symptomatic, not cytoreductive, therefore, to remove endometriosis lesions, surgery should be performed.

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