

ALTERNATIVE TREATMENT IN ENDOMETRIOSIS

Elena-Silvia NADĂ¹
Ovidiu Gabriel BRATU²
Diana MIHAI³
Elvira BRĂȚILĂ⁴

ABSTRACT:

ENDOMETRIOSIS IS A CHRONIC DISORDER CAUSING REDUCED QUALITY OF LIFE MAINLY DUE TO CHRONIC PELVIC PAIN. MEDICAL AND SURGICAL TREATMENT OPTIONS ARE NON-CURATIVE AND SOMETIMES HAVE ADVERSE EFFECTS. IN RECENT YEARS ALTERNATIVE TREATMENT HAS BECOME MORE AND MORE POPULAR DUE TO ITS FEWER SIDE EFFECTS. FRUIT AND VEGETABLE CONSUMPTION, ESPECIALLY ORGANIC, RED MEAT AND OMEGA 3 FATTY ACIDS HAVE SHOWN IMPROVEMENT IN THE PROGRESSION OF THE DISEASE. NATURAL SUPPLEMENTS SUCH AS SILYMARIN, MELATONIN, EVENING PRIMROSE OIL AND CERTAIN VITAMINS ARE ASSOCIATED WITH DECREASED LEVELS OF CHRONIC PELVIC PAIN. REGULAR PHYSICAL ACTIVITY AND ACUPUNCTURE REPRESENT A FEASIBLE APPROACH IN THE LONG RUN FOR THE ALLEVIATION OF CHRONIC PELVIC PAIN.

KEYWORDS: ENDOMETRIOSIS, DIET, VITAMINS, PHYSICAL EXERCISE, ACUPUNCTURE

¹ PhD student “Carol Davila” University of Medicine and Pharmacy Department of Obstetrics and Gynecology 8 Eroii Sanitari Str, 050474, Bucharest, Romania; Clinical Hospital of Obstetrics and Gynecology “Prof Dr Panait Sarbu”, Department of Obstetrics and Gynecology, Calea Giulesti, no 5, 060274, Bucharest, Romania elena_s_nada@yahoo.com

² PhD Clinical Department No. 3 “ Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania Department of Urology, “Dr.Carol Davila” Central Military Emergency University Hospital Bucharest, Romania, Academy of Romanian Scientists, Bucharest; ovi78doc@yahoo.com

³ PhD student “Carol Davila” University of Medicine and Pharmacy Department of Obstetrics and Gynecology 8 Eroii Sanitari Str, 050474, Bucharest, Romania; Clinical Hospital of Obstetrics and Gynecology “Prof Dr Panait Sarbu”, Department of Obstetrics and Gynecology, Calea Giulesti, no 5, 060274, Bucharest, Romania dr.dianamihai@gmail.com

⁴ PhD Professor “Carol Davila” University of Medicine and Pharmacy Department of Obstetrics and Gynecology 8 Eroii Sanitari Str, 050474, Bucharest, Romania; Clinical Hospital of Obstetrics and Gynecology “Prof Dr Panait Sarbu”, Department of Obstetrics and Gynecology, Calea Giulesti, no 5, 060274, Bucharest, Romania elvirabarbulea@gmail.com

INTRODUCTION

Endometriosis is a chronic gynecologic disorder affecting nearly 10-15% of child-bearing age women. It is strongly associated with a reduced quality of life due to its sometimes debilitating symptoms such as dysmenorrhea, dyspareunia, chronic pelvic pain, irregular bleeding and infertility. The most frequent locations for endometriotic lesions are the ovaries and pelvic peritoneum, while deep infiltrating endometriosis alters the anatomy of the uterosacral ligaments, pouch of Douglas, rectum and lower urinary tract. However, rare locations have been described in case reports, such as cerebral, pulmonary and even umbilical, as a primary location⁵.

Optimal evaluation of endometriotic lesions is crucial for choosing the appropriate treatment plan. Clinical examination and transvaginal ultrasound are readily available and suitable tools for diagnosis. Endometriomas are easily evaluated with transvaginal sonography, but it has lower sensibility and specificity when it come to deep infiltrating endometriosis. Several studies have pointed out the higher accuracy in evaluating the posterior pelvic compartment of the sonovaginography with ultrasound gel. Colorectal endometriosis cannot be detected at physical examination, especially when the lesions are extended above the sigmoid. But recently the evaluation of the small and large bowel endometriosis is possible with the use of magnetic resonance imaging in combination with computed tomography-based virtual colonoscopy⁶.

Treatment options available today, both medical and surgical, focus mainly on chronic pelvic pain and infertility, but are non-curative and often lead to recurrence after cessation or adverse reactions. The long term hormonal treatment often prescribed is progesterone, which is used only in order to avoid relapses. Several studies have revealed the importance of the immunohistochemical profile of the endometriotic lesion in order to assess the pathogenesis, therapeutic intervention and probability of relapse. Once again it is stated the importance of treatment individualization in endometriosis⁷. Current guidelines do not offer precise

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⁶ Brătilă E, Comandașu DE, Coroleucă C, Cârstoiu MM, Berceanu C, Mehedințu C, Brătilă P, Vlădăreanu S. Diagnosis of endometriotic lesions by sonovaginography with ultrasound gel. *Med Ultrason* 2016; 18: 469-474; Nada E-S, Brinduse L, Bratu O, Marcu D, Bratila E. Endometriosis-associated infertility. *Modern Medicine*, 2018, 25(3): 131-136.; Mehedințu C, Brîndușe L, Brătilă E, Monroc M, Lemercier E, Suaud O, Collet-Savoie C, Roman H. Does Computed Tomography-Based Virtual Colonoscopy Improve the Accuracy of Preoperative Assessment Based on Magnetic Resonance Imaging in Women Managed for Colorectal Endometriosis. *JMIG* 2018; 25: 1009-1017; Brătilă E, Comandașu D, Coroleucă C, Cîrstoiu M, Bohîlțea R, Mehedințu C, Vlădăreanu S, Berceanu C Gastrointestinal symptoms in endometriosis correlated with the disease stage. *ISI Proceedings XXXVIth National Congress of Gastroenterology, Hepatology and Digestive Endoscopy, Filodiritto Editore* 2016: 67-71; Bruja A, Brinduse L, Bratu O, Diaconu C, Bratila E. Methods of transvaginal ultrasound examination in endometriosis. *Modern Medicine*, 2018, 25(3): 111-116

⁷ Nada E-S, Brinduse L, Bratu O, Marcu D, Bratila E. Endometriosis-associated infertility. *Modern Medicine*, 2018, 25(3): 131-136; Brătilă E, Brătilă CP, Comandașu DE, Baușic V, Vlădescu CT, Mehedințu C, Berceanu C, Cârstoiu MM, Mitroi G, Stănculescu R The assessment of immunohistochemical profile of endometriosis implants, a practical method to appreciate the aggressiveness and recurrence risk of endometriosis. *Rom J. Morphol Embryol* 2015, 56(4): 1301-1307; Mehedințu C, Antonovici M, Brîndușe L, Brătilă E, Stănculescu R, Berceanu C, Bratu O, Pițuru S,

recommendations regarding the best treatment. Studies in the last decade are focusing upon lifestyle changes such as diet, vitamin and antioxidant supplementation and even acupuncture.

THE INFLUENCE OF DIET

Diet is considered an important risk factor for the development and progression of many chronic diseases such as hypertension, diabetes, cancer, but in recent studies it was also connected with endometriosis. Nutrient deficient diet interferes with DNA methylation, oxidative stress and result in epigenetic abnormalities, overexpression of estrogen receptor β and steroidogenic factor 1 leading to increased estradiol and prostaglandin levels, inflammations and cell growth⁸.

One of the path studied was the relationship between fruit and vegetable consumption and the risk of endometriosis. These are not only a source of antioxidants, but they also promote estrogen excretion. A large prospective ongoing cohort study, the Nurses' Health Study II, began in 1989 and included 116429 registered nurses aged 25-42 years who completed a questionnaire regarding food intake among other lifestyle, demographic and environmental information. Overall a greater intake of fruits and vegetables, especially >5 portions/day was associated with 18% lower risk for developing endometriosis in comparison with an intake of <2 portions/day. Even more, women eating up to 3 portions of fruits/ day had a 14 % lower disease risk than those consuming <1 portion/day. This was particularly observed with citrus fruits, especially oranges – 22% lower risk. In terms of vegetable consumption, there was no correlation with the risk of endometriosis. However, more than 1 portion/ day of cruciferous vegetables (cabbage, broccoli, cauliflower) lead to a 13% higher risk of endometriosis⁹. However fruits and vegetables rich in fiber and nutrients contribute to estrogen excretion, leading to hormonal regulation¹⁰.

The same aspect was pointed out in a study by Parrazini et al in 2004. This case-control study of 504 women aged 20-65 years revealed a lower risk of developing endometriosis in women consuming large amounts of fruits and green vegetables¹¹. In 2011 a study by Trabert reached a

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⁸ Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis Rev. Assoc. Med. Bras. Vol 61 no. 6 Sao Paulo Nov/Dec. 2015; Socea LI, Visan DC, Barbuceanu SF, Apostol TV, Bratu OG, Socea B. The antioxidant activity of some acylhydrazones with dibenzo[a,d][7]annulene moiety. Rev Chim (Bucharest), 2018, 69(4): 795-797

⁹ H. R. Harris, A. C. Eke, J. E. Chavarro, S. A. Missmer Fruit and vegetable consumption and risk of endometriosis Hum. Reprod. 2018 Apr; 33(4): 715-727

¹⁰ Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis Rev. Assoc. Med. Bras. Vol 61 no. 6 Sao Paulo Nov/Dec. 2015

¹¹ Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis Rev. Assoc. Med. Bras. Vol 61 no. 6 Sao Paulo Nov/Dec. 2015; H. R. Harris, A. C. Eke, J. E. Chavarro, S. A. Missmer Fruit and vegetable consumption and risk of endometriosis Hum. Reprod. 2018 Apr; 33(4): 715-727; Joanna Jurkiewicz-Przondziona, Magdalena Lemm, Anna Kwiatkowska-Pamula, Ewa Ziolkow, Mariusz K. Wojtowicz Influence of diet on the risk of developing endometriosis Ginekologia Polska 2017, vol 88, no. 2, 96-102

different conclusion: >2 portions/day of fruits was associated with a higher disease risk. This opposite result was explained by the presence of pesticides in fruits which are responsible for an increased level of oxygen reactive species, diminishing their antioxidant effect. However the consumption of fruits should not be discouraged, more than that, the organic fruit consumption should be preferred¹².

The same cohort from the Nurses' Health Study was analyzed to study the relationship between dietary fat consumption and endometriosis. Palmitic acid, trans-unsaturated fatty acids (fried foods, margarine, crackers) and diets rich in animal fat were associated with a greater risk, specifically a risk of 80% with palmitic acid intake. But long term intake of Omega 3 resulted in a lower risk of laparoscopically diagnosed endometriosis¹³. Omega 3 fatty acids reduce inflammation through prostaglandin E3 and E3 α thereby improving dysmenorrhea, while Omega 6 fatty acids promote inflammation through prostaglandins E2 and F2 α . A study from 2009 revealed less pain and inflammation after surgical management of endometriosis in women taking Omega 3 supplements¹⁴.

Alcohol seems to be a risk factor while caffeine consumption has not been clearly demonstrated. A study showed that caffeine increases estrogen and sex hormone binding globuline levels¹⁵.

A beneficial effect was linked with the consumption of low fat dairy products. A study from 2013 revealed that women consuming >3 portions/day had a 18% lower risk of developing endometriosis than those consuming 2 portions/day. This is also in connection with vitamin D plasma levels, which are inversely related with endometriosis occurrence¹⁶.

The influence of red meat, poultry, fish and seafood was investigated in several studies. Red meat was found to be have a major role in the development of endometriosis. It seems that the effect of red meat is independent of animal fat. The study conducted by Yamamoto found an increased risk in women eating >2portions/ day and a lower risk with 2-4 portions/ week , while replacement of red meat with fish or seafood led to a lower risk. One possible explanation for the detrimental effect of red meat is the heme iron content, which causes DNA damage and increases oxidative stress. Secondly, an intriguing fact is that women consuming larger amounts of red meat

¹² Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis Rev. Assoc. Med. Bras. Vol 61 no. 6 Sao Paulo Nov/Dec. 2015; Joanna Jurkiewicz-Przondziona, Magdalena Lemm, Anna Kwiatkowska-Pamula, Ewa Ziolkko, Mariusz K. Wojtowicz Influence of diet on the risk of developing endometriosis Ginekologia Polska 2017, vol 88, no. 2, 96-102

¹³ Bodean O, Bratu O, Bohiltea R, Munteanu O, Marcu D, Spinu DA, Vacaroiu IA, Socea B, Diaconu CC, Fometescu Gradinaru D, Cirstoiu M. The efficacy of synthetic oral progestin pills in patients with severe endometriosis. Rev Chim (Bucharest), 2018, 69(6): 1411-1415.; Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis Rev. Assoc. Med. Bras. Vol 61 no. 6 Sao Paulo Nov/Dec. 2015

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¹⁵ Joanna Jurkiewicz-Przondziona, Magdalena Lemm, Anna Kwiatkowska-Pamula, Ewa Ziolkko, Mariusz K. Wojtowicz Influence of diet on the risk of developing endometriosis Ginekologia Polska 2017, vol 88, no. 2, 96-102

¹⁶ Joanna Jurkiewicz-Przondziona, Magdalena Lemm, Anna Kwiatkowska-Pamula, Ewa Ziolkko, Mariusz K. Wojtowicz Influence of diet on the risk of developing endometriosis Ginekologia Polska 2017, vol 88, no. 2, 96-102

are expected to be overweight or obese because of the higher caloric intake which is contradictory to the literature which states that lower BMI is a risk factor for endometriosis¹⁷. Thirdly, red meat consumption increases estrogen levels and promotes inflammation through arachidonic acid. This omega 6 polyunsaturated fatty acid stimulates the synthesis of prostaglandins and leukotrienes¹⁸.

NUTRITIONAL SUPPLEMENTS

Vitamins A, C, D and E provide antioxidant effect leading to reduced inflammation and antiproliferative action. Analyzing the population from the Nurses' Health Study it appears that only food rich in these antioxidants (not supplements) lead to a lower risk of endometriosis. The same conclusion was reached by Mier-Cabrera who found an improvement in antioxidant markers after a four-month antioxidant rich diet¹⁹.

The consumption of vitamin B1, B9, C and E solely from food sources is inversely related to endometriosis risk. Vitamin C and E lower free radical and reactive oxygen species levels, which are involved in the proliferation and adhesion of endometrial cells in the peritoneal cavity. Vitamin B6 intensifies the estrogen metabolism into an inactive form and converts the linoleic acid into gamma linolenic acid, thereby increasing the level of anti-inflammatory prostaglandins²⁰.

Vitamin D suppresses COX-2 expression in the endometrium, thereby reducing IL-6 and prostaglandin levels, as well as prostaglandin receptor expression. A dose of 300,000 UI of vitamin D administered before the menstrual cycle led to a reduction in pain and nonsteroidal anti-inflammatory use in women with dysmenorrhea during a two month study²¹.

Vitamin C is also known for its antioxidant, anti-inflammatory and angiogenic effects. In an animal model study from 2013, administration of intravenous vitamin C was associated with a significant reduction in endometriotic implant volume compared with the placebo group. The same beneficial effect was observed upon endometriotic cysts. Oral supplements with high doses of vitamin C led to a significant reduction in endometriotic cyst volume and weight²². In another

¹⁷ Rosalia C. M. Simmen, Angela S. Kelley Seeing red: diet and endometriosis risk *Ann. Transl. Med.* 2018 Dec; 6(Suppl 2): S119

¹⁸ Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis *Rev. Assoc. Med. Bras.* Vol 61 no. 6 Sao Paulo Nov/Dec. 2015; Rosalia C. M. Simmen, Angela S. Kelley Seeing red: diet and endometriosis risk *Ann. Transl. Med.* 2018 Dec; 6(Suppl 2): S119

¹⁹ Gabriela Halpern, Eduardo Schor, Alexander Kopelman Nutritional aspects related to endometriosis *Rev. Assoc. Med. Bras.* Vol 61 no. 6 Sao Paulo Nov/Dec. 2015; Mier-Cabrera J, Aburto-Soto T, Burrola-Méndez S, Jiménez-Zamudio L, Tolentino MC, Casanueva E, et al. Women with endometriosis improved their peripheral antioxidant markers after the application of a high antioxidant diet. *Reprod Biol Endocrinol.* 2009; 7:54

²⁰ Anne Marie Darling, Jorge E. Chavarro, Susan Malspeis, Holly R. Harris, Stacey A. Missmer A prospective cohort study of Vitamins B, C, E and multivitamin intake and endometriosis *J. Endometr.* 2013 Jan 1; 5(1): 17-26

²¹ Lasco A, Catalano A, Benvenga S. Improvement of primary dysmenorrhea caused by a single oral dose of vitamin D: results of a randomized, doubleblind, placebo-controlled study. *Arch Intern Med.* 2012; 172:366-7.

²² Ozlem Ulas Erten, Tugba Altun Ensari, Berna Dilbaz, Huseyin Cakiroglu, Sadiman Kiykac Altinbas, Muzaffer Caydere, Umit Goktolga Vitamin C is effective for the prevention and regression of endometriotic implants in an experimentally induced rat model of endometriosis *Taiwan J Obstet Gynecol.* 2016 Apr;55(2):251-7; Y. Durak, A. Kokcu, M. Kefeli, D. Bildircin, H. Celik, T. Alper Effect of vitamin C on the growth of experimentally induced endometriotic cysts *J Obstet Gynaecol Res*, 39 (2013), pp. 1253-1258

study the vitamin C effect was greater among smokers, than non-smokers. Controversy, smoking found to have a protective effect upon endometriosis through the reduction of estrogen levels²³.

A randomized placebo-controlled study conducted in the USA evaluated the effects of vitamin E (1200UI) and vitamin C (1000mg) compared with placebo during 8 weeks. The results showed a reduction in chronic pelvic pain, dysmenorrhea and dyspareunia (43%, 37% and 24% respectively) compared with the placebo group. There was also a reduction in inflammatory markers in the peritoneal fluid at the end of the treatment²⁴.

Magnesium and phosphorus intake have also been studied in relation with endometriosis. Magnesium has a beneficial effect upon retrograde menstruation by reducing the smooth muscle contractility of the fallopian tubes. Low magnesium levels were found in women with history of miscarriages and with premenstrual syndrome. But high magnesium and phosphorus intake have inverse relationship with endometriosis risk and are associated with lower levels of inflammatory markers in the peritoneal fluid, such as IL-6 and TNF α ²⁵.

Evening primrose oil is a well known natural remedy for breast pain, premenstrual syndrome, but also for endometriosis and irritable bowel syndrome. Its effect is based upon an omega-6 fatty acid, gamma-linolenic acid which is converted into anti-inflammatory prostaglandins. So evening primrose oil relieves menstrual cramps, reduces breast tenderness associated with premenstrual syndrome, irritable bowel flare-ups and controls endometriosis-associated inflammation. However there can be minor side effects, such as headaches and nausea²⁶.

Silymarin is an extract from the dried fruits of milk thistle, is well known for its antioxidant effect and is used mainly in case of toxic liver damage or as an adjunct therapy in chronic hepatitis and cirrhosis. In animal model studies it has proven to be a cell membrane stabilizer, thereby inhibiting cells' damage. In a recent article from 2018 published in the Taiwanese Journal of Obstetrics and Gynecology the effect of silymarin, cabergoline and letrozole was studied on induced endometriosis in a rat model. There were four study groups divided upon their medication, the fourth group being the control one. After 3 weeks the results revealed that the mean volume of the implants and the histopathological score decreased significantly in the silymarin, letrozole and cabergoline group, respectively, compared to the control group. The total antioxidant activity was also measured in the serum and peritoneal fluid and was found to be higher in the silymarin group²⁷.

²³ Anne Marie Darling, Jorge E. Chavarro, Susan Malspeis, Holly R. Harris, Stacey A. Missmer A prospective cohort study of Vitamins B, C, E and multivitamin intake and endometriosis *J. Endometr.* 2013 Jan 1; 5(1): 17-26

²⁴ N. Santanam, N. Kavtaradze, A. Murphy, C. Dominguez, S. Parthasarathy Antioxidant supplementation reduces endometriosis-related pelvic pain in humans *Transl Res*, 161 (2013), pp. 189-195

²⁵ Holly R. Harris, Jorge E. Chavarro, Susan Malspeis, Walter C. Willet, Stacey A. Missmer Dairy-Food, Calcium, Magnesium, and Vitamin D Intake and Endometriosis: A Prospective Cohort Study *Am J. Epidemiol.* 2013 Mar 1; 177(5): 420-430

²⁶ J. Kleijne Evening primrose oil *BMJ* 1994 Oct 1; 309(6958): 824-825; Bayles B, Usatine R Evening primrose oil *Am. Fam. Physician.* 2009 Dec 15; 80(12): 1405-8

²⁷ Jouhari S, Mohammadzadeh A, Soltangharae H, Mohammadi Z, Khazali S, Mirzadegan E, Lakpour N, Fatemi F, Zafardoust S, Mohazzab A, Naderi MM. Effects of silymarin, cabergoline and letrozole on rat model of endometriosis *Taiwan J Obstet Gynecol.* 2018 Dec;57(6):830-835.

The effects of silymarin have also been studied in the field of infertility. Beneficial evidence was revealed with regard to early granulosa cell apoptosis²⁸ as well as protective effects on ovarian reserve and sperm motility²⁹. There are no side effects associated with the use of silymarin.

Melatonin is particularly used as a sleep supplement and is naturally produced by the pineal gland at night. Recently, melatonin is also used for analgesic, antioxidant and anti-inflammatory properties. In a study of 40 women with chronic pelvic pain, aged 18-45 years, the administration of 10mg of melatonin daily for 8 weeks produced remarkable results: overall 80% reduction in the need for analgesics, reduced chronic pelvic pain by 39.80%, reduced dysmenorrhea by 38.01%, reduced dysuria and dyschezia and, of course, improved sleep quality³⁰.

A study published in the Journal of Reproductive Medicine revealed the beneficial effect of pycnogenol, a French maritime pine bark extract, as a natural remedy for endometriosis. 58 women surgically diagnosed with endometriosis were followed at 4, 12, 24 and 48 weeks after conservative surgery. 32 women were included in the pycnogenol and took 60 mg/ day for 48 weeks and 26 women were administered gonadotropin-releasing agonist. Results showed that women taking pine bark extract experienced a 33% reduction in pain, including severe pain, which persisted without relapse, unlike the gonadotropin-releasing group³¹.

PHYSICAL ACTIVITY

Regular physical activity is known to have a protective effect in the progression of diseases which have an inflammatory component such as type 2 diabetes, inflammatory bowel disease, colon and breast cancer and so is the case of endometriosis. Physical exercise performed on a regular basis has numerous valuable effects: increases the level of cytokines with anti-inflammatory and antioxidant properties, increases sex-hormone binding globulin level, thereby decreasing estrogen's bioavailability, reduces insulin resistance and hyperinsulinemia, reduces menstrual flow³².

Although studies available regarding the beneficial effect of physical activity as a risk factor or as a part of treatment plan are scarce a few conclusions have been drawn: the positive effect is limited to women starting physical exercise before 26 years for minimum 2 hours/week,

²⁸ N. Moosavifar, A.H. Mohammadpour, M. Jallali, G. Karimiz, H. Saberi Evaluation of effect of silymarin on granulosa cell apoptosis and follicular development in patients undergoing in vitro fertilization East Mediterr Health J, 16 (2010), pp. 642-645

²⁹ Jouhari S, Mohammadzadeh A, Soltanghorae H, Mohammadi Z, Khazali S, Mirzadegan E, Lakpour N, Fatemi F, Zafardoust S, Mohazzab A, Naderi MM. Effects of silymarin, cabergoline and letrozole on rat model of endometriosis Taiwan J Obstet Gynecol. 2018 Dec;57(6):830-835;

Y.C. Chen, L.C. Pan, C.W. Lai, Y.S. Chien, T.H. Wu Silymarin and protein kinase A inhibitor modulate glucose-mediated mouse sperm motility: an in vitro study Reprod Biol, 15 (2015), pp. 172-177

³⁰ Schwertner A, Conceicao Dos Santos CC, Costa GD, Deitos A, de Souza A, de Souza IC, Torres IL, da Cunha Filho JS, Caumo W. Efficacy of melatonin in the treatment of endometriosis: a phase II randomized, double-blind, placebo-controlled trial. Pain. 2013 Jun; 154(6): 874-81

³¹ Kohama T, Herai K, Inoue M. Effect of French maritime pine bark extract on endometriosis as compared with leuprorelin acetate J. Reprod Med. 2007 Aug; 52(8): 703-8

³² Camila M. Bonochoer, Mary L. Montenegro, Julio C Rosa e Silva, Rui A Ferriani, Juliana Meola Endometriosis and physical exercises: a systematic review Reprod Biol Endocrinol. 2014; 12: 4; Laura Buggio, Giussy Barbara, Federica Facchin, Maria Pina Frattaruolo, Giorgio Aimi, Nicola Berlanda Self-management and psychological-sexological interventions in patients with endometriosis: strategies, outcomes, and integration into clinical care Int J. Womens Health. 2017; 9: 281-293

and as a prevention method, intense physical exercise should not be performed in the menstrual period. Of particular interest for women taking gonadotropin-releasing agonist treatment, physical activity is an additional therapy in the recovery of bone density³³.

Yoga, defined by the World Health Organization, as a mind and body practice is able to reduce stress, strengthen musculature and alleviate symptoms of numerous chronic diseases through a combination of contemplative techniques, breathing and meditation exercises and specific postures. A study which included 15 women with symptomatic endometriosis who attended yoga practice for 8 weeks reported an overall positive effect upon pelvic pain, in addition to improved self-awareness and self-esteem³⁴.

ACUPUNCTURE

Acupuncture implies the insertion of fine metallic needles into the skin at specific sites and the Chinese traditional medicine promotes it as a technique for balancing the Yin and Yang, strengthening body's resistance to disease. It has the ability to interfere with pain mechanisms, inducing changes in the central nervous system leading to a reduction of perceived pain level. One of the mechanisms is the release of endogenous opioids in brain stem, subcortical and limbic structures leading to obstruction of brain structures involved in the transmission of pain and activation of endogenous descending pain inhibitory pathways. And secondly, acupuncture prompts production of cortisol and adenocorticotrop hormone from the pituitary gland leading to an anti-inflammatory effect³⁵.

Although it is still a controversial technique, is it more and more used as a long term pain management option with no adverse effects when performed by a skilled therapist. A meta analysis published in the Journal of Pain Research included 99 women diagnosed with endometriosis who underwent acupuncture. The number of treatment varied from 9 to 16, the needle retention time was 15-20 minutes and the acupuncture points were the lower pelvic region and back, lower abdominal area, hands and feet. After treatment, all women reported lower pain score levels, increased health-related quality of life and decreased analgesic intake and noticeable stress level³⁶.

PSYCHOLOGICAL AND SEXUAL INTERVENTIONS

Endometriosis has a long-term negative effect upon women's psychological health and quality of life. The multidisciplinary team involved in the treatment of these patients should also include a psychologist and a sexual therapist. Due to its chronic status, numerous and complex therapeutic options, uncertain prognosis and threat of infertility, women with endometriosis

³³ Camila M. Bonoche, Mary L. Montenegro, Julio C Rosa e Silva, Rui A Ferriani, Juliana Meola Endometriosis and physical exercises: a systematic review *Reprod Biol Endocrinol*. 2014; 12: 4

³⁴ Laura Buggio, Giussy Barbara, Federica Facchin, Maria Pina Frattaruolo, Giorgio Aimi, Nicola Berlanda Self-management and psychological-sexological interventions in patients with endometriosis: strategies, outcomes, and integration into clinical care *Int J. Womens Health*. 2017; 9: 281-293

³⁵ Laura Buggio, Giussy Barbara, Federica Facchin, Maria Pina Frattaruolo, Giorgio Aimi, Nicola Berlanda Self-management and psychological-sexological interventions in patients with endometriosis: strategies, outcomes, and integration into clinical care *Int J. Womens Health*. 2017; 9: 281-293; Irene Lund, Thomas Lundeberg Is acupuncture effective in the treatment of pain in endometriosis? *J. Pain Res*. 2016; 9: 157-165

³⁶ Irene Lund, Thomas Lundeberg Is acupuncture effective in the treatment of pain in endometriosis? *J. Pain Res*. 2016; 9: 157-165

develop anxiety and depression which could negatively interfere with the course of treatment. Mindfulness psychological interventions, individual or group session, counseling, patient education taking into account all aspects of female sexuality, all lead to an overall long-lasting improvement on health-related quality of life³⁷.

CONCLUSION

Endometriosis is a chronic condition with a multifactorial etiology which benefits from a complex treatment, both medical and surgical. More and more attention is drawn nowadays to lifestyle and dietary interventions. The consumption of fruit and vegetables, especially organic, has a beneficial impact on the progression of the disease. Also, natural supplements, dairy products rich in calcium and vitamin D and omega 3 fatty acids decrease the risk of endometriosis.

Therapies aiming at diminishing pain such as yoga and acupuncture show promising results, but more randomized studies are necessary to evaluate different treatment strategies in order to maximize the benefits of these alternative medical treatments.

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