Nutrition in Endometriosis

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Endometriosis is a chronic, painful, estrogen-related inflammatory disease that affects approximately 10% of the female population. Endometriosis has a significant negative impact on quality of life. Nutrition may be involved in the development and severity of endometriosis.

endometriosis nutrition anti-inflammatory diet antioxidants pelvic pain

1. Vegetables and Fruit

1.1. Polyphenols

Numerous studies provide solid evidence of positive health effects of eating a diet rich in vegetables and fruits, because of the existence of the bioactive plants' composites, especially polyphenols. Polyphenols have proven anti-cancer, anti-inflammatory, anti-atherosclerotic, antioxidative and anti-hypertensive properties [1]. The anti-inflammatory potential of natural dietary polyphenols might be used in the management of endometriosis as an inexpensive, non-toxic and readily available agent [2]. Several studies indicate an inverse correlation between polyphenol application, such as phytoestrogens and female cancer risk [3][4][5].

1.2. Phytoestrogens

Phytoestrogens (PE) are naturally occurring plant compounds which are structural and functional homologies with estrogen. There are three classes of PE: lignans, stilbenes, and flavonoids [6]. Phytoestrogens are found in vegetables, fruits, tea, grains, beans, sprouts, soybean, oilseeds and cabbage. PE are very similar in structure to estrogen, and, owing to that similarity, they can function as weak estrogenic factors interfering with molecular and hormonal signaling, which prevents the advancement of non-insulin-dependent diabetes, cancer, obesity, cardiovascular diseases and negative menopausal symptoms [6]. Phytoestrogens could link to estrogen receptor (ER) and affect ER-mediated responses [7]. A lot of case–control studies investigated connection in the midst of PE ingestion and endometriosis risk. A comparison of PE consumption by 78 patients with laparoscopically proven EMS versus 78 healthy women by Youseflu et al. shows that the intake levels of isoflavones and lignans were inversely correlated with endometriosis risk [8]. In a systematic review by Bartiromo et al., 19 out of 22 studies indicated the capability of phytoestrogens to generate proapoptotic, anti-inflammatory, anti-proliferative outcomes on cultured cells [6].

1.3. Resveratrol

Among the most known and tested polyphenols, whose beneficial influence on health was proven in in vitro and in vivo models and in clinical tests, is resveratrol (RSV). More than 70 types of plants and plant-based products, principally black and red grapes, red wine, berries and nuts, comprise RSV, which is a phytoalexin and a phytoestrogen [2][9][10].

A number of in vitro tests [11][12][13][14][15][16] have investigated the impact of RSV on endometrial and endometriotic cells and have demonstrated a pro-apoptotic function and inhibitory effect on cell proliferation and invasive growth. These effects can be partially explained by inhibitory effect on the expression of insulin-like growth factor-1 (IGF-1), surviving and hepatocyte growth factor (HGF), while its effects on estrogen are more complex.

In vivo models of EMS have confirmed both the pro-apoptotic, anti-invasive role and also an inhibitory impact on angiogenesis, which is related to a drop in the expression of pro-invasive, pro-angiogenic and pro-inflammatory factors, particularly interleukin-6 (IL-6) and interleukin-8 (IL-8) [13][17][18][19].

The clinical studies [20] on the combination of oral contraception with RSV have informed potentially positive results in a treatment of endometriosis-related symptoms: decreased dysmenorrhea and pain relief; however, the number of studies is insufficient [10].

A clinical trial of Mendas et al. showed no positive effects of resveratrol consumption [21]. RSV proved its efficiency either alone or in combination with other substances used in EMS therapy such as statins or leuprolide acetate [2].

1.4. Vitamins C

Vitamin C, among the most important antioxidatives, strongly reduces free radicals. Humans are incapable of synthesizing vitamin C, so it should be provided with food or in the form of supplements/medications. Peppers, citrus, kiwi, broccoli, tomatoes, potatoes and strawberries are some of the products renowned for their high content of vitamin C [22].

Hoorsan et al., in their experiment on mice, suggested that vitamin C has considerable importance for improving the fecundity function of ovaries and reducing the induction and growth of endometrial implants [23].

A randomized, triple-blind placebo-controlled clinical study of Amini et al. with the supplementation of vitamins C and E confirmed the effect of lowering the systemic indicators of oxidative stress in patients with EMS [24].

Ansariniya et al., in a lab trial, determined the influence of vitamins C and E on VEGF gene expression and production in peritoneal macrophages of women with endometriosis in comparison with the control group. It was found that vitamins C and E, at different incubation times and concentrations, changed the expression of the VEGF gene in the peritoneal macrophages but they had no effect on the production of VEGF [25].

2. Spices and Herbs

According to the definition proposed by the Food and Drug Administration (FDA), spices are: “aromatic vegetable substances, in the whole, broken, or ground form, whose significant function in food is seasoning rather than nutrition” [26]. Herbs and spices, such as oregano, rosemary, thyme and parsley, contain high levels of polyphenols, especially phenolic acids and flavonoids [27]. There are many herbs with known or potential significant anti-inflammatory activity. The spices with the most known anti-inflammatory effect are: thyme, oregano, basil, rosemary, mint, sage, curcuma, dill, cinnamon, parsley, clove, lemon grass, nutmeg, ginger, fenugreek, pepper and chili pepper [27][28][29][30][31][32][33].

Many of the anti-inflammatory substances (such us capsaicin, gingerol, and curcumin) in spices and herbs inhibit one or more of the steps linking pro-inflammatory stimuli with cyclooxygenase (COX) activation [27].

Curcuma (also known as turmeric) is a spice with proven anti-inflammatory and anti-cancer properties. It reduces the concentration of estrogens, TNF alpha and interleukin mediators, accelerates cellular apoptosis, and inhibits angiogenesis [29][34][35]. Consuming turmeric in conjunction with black pepper (containing piperine) increases the bioavailability of curcumin by up to 2000% [36].

In the studies of Fadin et al., a marked reduction in pain associated with endometriosis and the use of smaller amounts of non-steroidal anti-inflammatory drugs was observed in women supplemented with 200 mg of quercetin, 210 g of Curcuma longa’s dry extract and 150 mg of acetylcysteine for 2 months [37].

3. Tea and Coffee

White and green tea contain more catechins (substances classified as polyphenols) with strong antioxidant properties compared to black tea. White tea comprises minerals, proteins, amino acids, caffeine, gallic acid and catechins [38].

Meta-analysis suggests that caffeine intake of less than 300 mg/day is not linked with a higher EMS development risk. Higher caffeine consumption may be related to the development of the disease, but there is a shortage of well-designed, large-scale clinical trials to explain this relationship and the relevance of caffeine in the pathophysiology of EMS [39].

Caffeic acid, a polyphenol present, e.g., in coffee, some vegetables and legumes, reduces oxidative stress, which can alleviate complications from endometriosis [40].

4. Dairy Food

Dairy is a good source of progesterone, estrogen, calcium, vitamin D, anti-inflammatory and anti-tumorigenic ingredients, polyunsaturated fatty acids (PUFAs) and butyric acid [8].

There are some hypotheses regarding potential biochemical and physiological effects of dairy on the risk of developing EMS. Among them is that a high consumption of calcium-rich dairy products may reduce inflammatory and oxidative stress by decreasing inflammatory factors: tumor necrosis factor-a (TNF-a), reactive oxygen species and IL-6 [41]. An inverse relationship between the level of vitamin D and C-reactive protein was observed in atherosclerosis vascular disease and diabetes mellitus, which may suggest a similar relationship in endometriosis [41].

In a case–control study of Iranian Women, it was found that higher dairy intake is connected with a reduced risk of EMS [8]. Additionally, the longitudinal cohort study by Nodler et al. demonstrated that adolescents who consumed larger portions of dairy, including yoghurt and ice cream, had a lower rate of endometriosis recognition in adulthood [41].

A Dose–Response Meta-Analysis by Qi et al. showed that significant effects of reducing endometriosis were obtained with a daily consumption of ≥3 servings of dairy products. That study also analyzed a relationship between endometriosis and particular types of dairy—the heavy consumption of high-in-fat dairy and cheese might result in a decrease of EMS risk, while high butter consumption may lead an increased risk of endometriosis [42].

5. Fish

Fish oil has been shown to decrease circulating levels of series 2 prostaglandins and decrease dysmenorrhea and inflammatory symptoms [43].

5.1. Omega 3 and Omega 6

Polyunsaturated fatty acids (PUFAs) are fatty acids containing a minimum of two double bonds. Omega 3 (*n*-3) and omega 6 (*n*-6) PUFAs are found in fatty fish and seed/vegetable oils [44].

Akyol et al., in a randomized, single-blind, prospective and controlled experimental trial on female rats, observed that omega 3 caused a considerable recession of endometriotic implants [45]. In a clinical trial by Nodler et al., a reduction in pelvic pain in women with endometriosis who complemented fish oil rich in omega 3 was noted; however, a similar result was noticed in the placebo group [46].

A cross-sectional research by Hopeman et al. [44] examined samples and data from women undergoing in vitro fertilization (IVF) with surgically proven endometriosis and from women without endometriosis to ascertain if there is a relationship with serum omega 3 PUFAs α-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) or *n*-6 PUFAs linoleic acid (LA) and arachidonic acid (AA) and endometriosis. This study showed that patients with higher serum EPA levels were at 82% less risk of EMS development in contrast with patients with low EPA levels, while no association between total PUFAs, total omega 3 PUFAs, or total omega 6 PUFAs and EMS was found [44].

In the controlled experimental study of female rats, Pereira et al. demonstrated that the omega 6/3 and omega 9/6 nutraceuticals diminished pain associated with endometriosis, but did not improve fertility [47].

5.2. Vitamin D

Fatty fish and cod liver oil contain vitamin D3 (cholecalciferol) and its metabolite, 25(OH)D3, a fat-soluble secosteroid hormone that plays a significant role as a immunomodulatory and anti-proliferative mediator. The best source of vitamin D is skin synthesis, which occurs under the influence of the activity of ultraviolet B radiation [22] [48].

Vitamin D receptors and metabolizing enzymes are found in the endometrium and ovaries of women with and without EMS, and it is assumed that cholecalciferol might affect immune cells in the local environment [22].

In the randomized, double-blind, placebo-controlled study in 60 women with endometriosis, it was shown that regular cholecalciferol intake in women resulted in a considerable increase in total−/HDL-cholesterol ratio and hs-CRP and TAC levels and pelvic pain, but this had no influence on metabolic profiles and further clinical manifestations [49].

In an evidence-based critical appraisal of vitamin D in reproduction, Lagana et al. suggested that the supplementation of vitamin D should be carefully evaluated, considering the pleiotropic actions in diverse microenvironments of the body as well as the different sources of dietary intake and synthesis [48]. EMS is related to a normal or high 25(OH)D reserve, which may be due to an equalizing mechanism controlling inordinate local inflammation commonly noticed in women with endometriosis. However, endometriosis patients report a meaningful decrease in the pelvic pain during supplementation of vitamin D [50].

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