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The influence of selected food ingredients on the reduction of the risk of endometriosis: a literature review

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ABSTRACT

Endometriosis is a common disease that occurs in 6-10% of women of reproductive age. The disease is often associated with chronic pelvic pain and infertility. Endometriosis is an inflammatory disease and is estrogen dependent. Its definition is the presence of endometrial-like tissue outside the uterus. The etiology of the disease remains unclear. It is believed that a variety of immunological, genetic, hormonal, and environmental factors may be responsible for the development of endometriosis. Surgical confirmation of the presence of endometrial tissue outside the uterus is necessary for the diagnosis of endometriosis. For this reason, endometriosis is considered to be underdiagnosed. Currently, available treatments have many limitations and cause many side effects during their long-term use. For this reason, other treatment and prevention methods for this disease are being sought. Research on the influence of dietary factors on endometriosis allows concluding that diet and particular food ingredients can be considered a factor reducing the risk of endometriosis. Therefore, understanding the role of nutrition in the development of endometriosis is of great importance for the development of effective guidelines related to the prevention of this disease. Therefore, we have reviewed the available literature related to the impact of individual components of the daily diet on the risk of developing endometriosis. Omega-3 fatty acids, dairy products, and soy in particular appear to be promising dietary factors that could potentially reduce the risk of endometriosis. Further research is needed to solidify this knowledge.

INTRODUCTION AND PURPOSE

Endometriosis is a proliferative disease in which endometrial tissue occurs in ectopic locations, most commonly in the pelvic cavity and ovaries. Endometriosis is a hormone-dependent and hormone-sensitive disease accompanied by a chronic inflammatory reaction. The most common symptoms are chronic pelvic pain, dysmenorrhea, irregular uterine bleeding, and dyspareunia. Endometriosis significantly affects female fertility and may cause infertility. It is estimated that the number of women of reproductive age suffering from this disease is about 6-10%. It is also estimated that it affects about 50% of patients struggling with the problem of infertility or pelvic pain syndrome. Despite the existence of many theories, the final etiology of the disease has not yet been clarified. Its occurrence and development are believed to be influenced by several pathogenetic factors - genetic, menstrual, environmental, and lifestyle factors. The diagnosis of endometriosis requires laparoscopic confirmation of the presence of endometrial-like tissue outside the uterus. Consequently, endometriosis remains underdiagnosed and it often takes several years from the onset of symptoms to the final diagnosis. Due to the different locations of the ectopic endometrial foci, there is no one effective treatment for all forms of endometriosis. Currently, pharmacological methods and various surgical techniques are used in therapy. There are also reports that women with endometriosis have a higher risk of developing autoimmune diseases and certain cancers such as breast and ovarian cancer. Endometriosis is a debilitating disease that significantly worsens the quality of life of an individual patient. Serious health problems related to endometriosis are prompting more research into prevention and treatment. In recent years, the role of nutrition in the process of the prevention, formation, and development of endometriosis has become the subject of interest in the scientific community, as it has been observed that diet and specific food components can affect the incidence of inflammation,

estrogen activity and the cyclicality of menstruation. This article aims to evaluate the literature data in terms of the correlation between individual food ingredients and reducing the risk of developing endometriosis. [1–4]

FRUIT AND VEGETABLE

It is believed that oxidative stress may be involved in the development of endometriosis, which is associated with the creation of a pro-inflammatory environment. This can lead to increased adhesion and growth of endometrial cells in the peritoneal cavity. A protective factor against too high concentrations of free radicals are antioxidants, which, apart from being formed in the body, can be taken with food. Depending on the type, fruit and vegetables are a source of many antioxidants and vitamins that can reduce the phenomenon of oxidative stress. [5]

Three studies analyzed the relationship between a daily or weekly consumption of fruit and vegetables and the risk of developing endometriosis. In a study by Harris et al. (2018), a non-linear, inverse relationship was found between increased fruit consumption and the risk of endometriosis ($p = 0.005$). This relationship was especially visible for citrus fruit. Women who consumed at least one serving of citrus fruit per day had a 22% lower risk of developing endometriosis (95% CI = 0.69-0.89; $p = 0.004$) compared to women who consumed <1 serving per week. Additionally, women who consumed one or more servings of cruciferous vegetables daily had a 13% higher risk of developing endometriosis (95% CI = 0.95-1.34; $p = 0.03$) compared to women who consumed <1 a portion per week. [6]

In a study by Parazzini et al. (2004), a significant reduction in the risk of endometriosis was observed in women consuming larger amounts of green vegetables (for the high consumption - OR 0.3, 95% CI = 0.2-0.5, p = 0, 0001) and fresh fruit (OR 0.6, 95% CI = 0.4–0.8, $p = 0.002$). [7]

In turn, a case-control study by Trabert et al. (2011) showed that an increased daily number of fruit servings was associated with an increased risk of disease (two or more servings) OR 1.5, 95% CI = 1.2-2.3, $p = 0.04$. A similar relationship was not observed for vegetable consumption.[8]

Vegetables and fruits can also be a source of organochlorine compounds, which in turn are responsible for increasing the risk of endometriosis. They are believed to exert pleiotropic effects via estrogen and androgen receptors and consequently disrupt endocrine pathways. [4]

DAIRY PRODUCTS

There are conflicting reports about the consumption of dairy products and their health effects, ranging from increasing inflammation to reducing inflammation. Recently published studies, including a systematic review of 16 studies (Ulven et al. 2019), documented significant anti-inflammatory effects. There are also reports that consuming dairy products and calcium reduces oxidative stress. [9–11]

A meta-analysis of seven studies by Qi et al. (2021) showed that total consumption of dairy products was inversely related to the risk of endometriosis, and the risk was reduced when dairy consumption exceeded 21 portions per week (RR 0.87, 95% CI 0.76-1.00; p = 0.04). Also, people who consumed more than 18 servings of high-fat dairy products a week had a lower risk of endometriosis. A product-specific study showed that cheese consumption was responsible for the reduction in risk (RR 0.86, 95% CI 0.74–1.00). However, a meta-analysis showed a higher risk of endometriosis associated with the consumption of large amounts of butter (1.27, 95% CI 1.03–1.55). [12]

A study by Nodler et al. (2020) to assess the relationship between the consumption of dairy products during adolescence and the risk of endometriosis, showed that women consuming more than four servings of dairy products per day during adolescence had a 32% lower risk of endometriosis in adulthood (95% CI = 0.47-0.96; p = 0.04) compared to women who consumed one serving or less per day. Yogurt and ice cream were associated with the lowest risk of developing endometriosis. [13]

A study by Samaneh et al. (2019) also showed that women with higher dairy consumption had a lower risk of endometriosis ($p < 0.05$). [14]

In a study by Harris et al. (2013), consumption of milk and other low-fat dairy products was associated with a lower risk of endometriosis. Women who consumed more than three servings of dairy products per day had an 18% lower risk compared to women who consumed two or fewer servings per day. In addition, it was shown that in women with a higher concentration of vitamin 25 (OH) D, the risk of endometriosis was reduced by 24% compared to women with lower concentrations. [15]

POLYUNSATURATED FATTY ACIDS AND FISH OILS

Polyunsaturated fatty acids (PUFAs) are fatty acids that contain 2 or more double bonds in their structure. Their classification depends on the position of the last double bond. Omega 3 (n-3 PUFA) acids are found primarily in fish and some plants and include ALA - α-linolenic acid, EPA - eicosapentaenoic acid, and DHA - docosahexaenoic acid. Omega 6 (n-6 PUFA) acids can be found in vegetable oils, meat, and eggs and include LA - linoleic acid, AA - arachidonic acid, and GLA – gamma-linolenic acid. DHA and EPA are compounds with a direct anti-inflammatory effect. They reduce the concentration of inflammatory mediators such as IL-6, IL-1β, and TNF-α. Omega-6 fatty acids, on the other hand, have the opposite effect and are pro-inflammatory.[1617,18]

In a study by Hopeman et al. (2015) in a group of 205 women who underwent in vitro fertilization (IVF) in the past, it was shown that women with high EPA serum levels were 82% less likely to develop endometriosis than women with low EPA levels (OR 0.18, 95% CI 0.04-0.78). [16]

In a study by Missmer et al. (2010), it was observed that in women who consumed the most omega-3 fatty acids with the highest fifth chain length, the likelihood of endometriosis was

22% lower compared to women who consumed the lowest fifth amount of omega-3 fatty acids (95% CI 0.62-0.99; p = 0.03). [19]

A study by Khanaki et al. (2012) aimed at comparing serum phospholipid fatty acid profiles in endometriosis patients with a control group and examining the correlation of this profile with disease severity, showed that the ratio of EPA to AA levels was a significant factor indicating the severity of the disease. [20]

A study by Gazvani et al. (2001) investigating the effect of PUFAs on the proliferation of endometrial cells in vitro and their production of interleukin-8 (IL-8), showed that in the presence of high concentrations of omega-3 endometrial cell survival from women with endometriosis was significantly reduced. [21]

In addition, studies are emerging to investigate the use of PUFAs in the treatment of endometriosis. In a study by Akyol et al. (2016) in rats with surgically induced endometriosis, it was shown that in the group receiving omega-3 acids, significant regression of endometrial implants (p = 0.02), a decrease in the level of interleukin-6 (IL-6) (p = 0.02) was observed, tumor necrosis factor-alpha (TNF-α) (p = 0.03) and vascular endothelial growth factor (VEGF) (p = 0.03). [22] Also in the study by Tomio et al. (2013), mice treated with EPA showed a reduction in the number of lesions. [23]

SOY

Soybeans contain many active ingredients, including soy protein, lecithin, and soy isoflavones. The isoflavones in soy are believed to have an anti-estrogenic effect. Their structure resembles that of estrogens. For this reason, research is ongoing on the use of these compounds in the prevention and treatment of estrogen-dependent diseases. There are also reports on the anti-cancer activity of soy isoflavones. They are believed to inhibit the activities of enzymes such as tyrosine kinase and topoisomerase II. [24]

The study by Sutrisno et al. (2018) aimed to investigate the effect of genistein on estrogen receptor modulation, inhibition of inflammation, and angiogenesis in a mouse model of peritoneal endometriosis. Genistein has been shown to modulate estrogen-α and estrogen-β receptors in the development of inflammation and angiogenesis in the investigated model, making it a potential candidate for the treatment of endometriosis. [25]

The study by Takaoka et al. (2018) investigated the in vitro and in vivo effects of daidzein-rich isoflavone aglycones (DRIA) and dietary supplements on cell proliferation in endometriosis, with results that DRIA inhibits proliferation in endometriosis. [26]

A study by Tsuchiya et al. (2007) in Japan investigated the relationship between consumption of soy isoflavones, estrogen receptor 2 gene polymorphisms, and the risk of endometriosis. It has been shown that women with higher levels of genistein and daidzein in their urine had a lower risk of advanced endometriosis (p = 0.01). [27]

CONCLUSIONS

The relationship between certain diseases, such as type 2 diabetes, obesity and hypertension, and diet has been scientifically proven. Therefore, it was possible to create dietary guidelines and nutritional recommendations for the prevention and treatment of these diseases. The question is whether diet may also affect the risk of endometriosis. Unfortunately, the data in the literature available at the moment are sparse and insufficient to formulate unambiguous relationships. The results of the conducted research often present contradictory results.

Endometriosis is a multifactorial disease with an unknown etiology at the moment. Many theories are trying to explain the biological mechanisms and then the influence of specific food ingredients on the risk of endometriosis. Due to the multi-stage process of endometriosis development, it should also be considered that different nutrients may have different effects at different stages of the disease development.

Endometriosis is a multifactorial disease with as yet unexplained etiology. There are several theories explaining the biological mechanisms by which selected food components may act and, as a result, reduce the risk of endometriosis. As this disease develops in several stages, the potential influence of different components on different stages of its development should also be considered.

Based on this review, dairy products, omega-3 fatty acids, and soy and its compounds are particularly promising dietary factors that have shown a potential reduction in the risk of endometriosis in all of the studies described. Unfortunately, the data on the consumption of vegetables and fruit are ambiguous and it cannot be clearly stated whether they are a protective factor in the examined aspect.

A summary of the findings of the literature review on the effect of selected food ingredients on the risk of endometriosis shows in Table 1.

Food ingredient	Effect on the risk of endometriosis
Fruit	↓ risk: Harris et al. (2018) ↑ risk: Trabert et al. (2011)
Vegetables	↓ risk: Parazzini et al. (2004) (especially green vegetables) ↑ risk: Harris et al. (2018) (cruciferous vegetables)
Dairy products	↓ risk: Qi et al. (2021)*, Nodler et al. (2020), Samaneh et al. (2019), Harris (2013) *excluding butter
Polyunsaturated fatty acids and fish oils	↓ risk: Hopeman et al. (2015), Missmer et al.

	(2010), Gazvani et al. (2001)
Soy	↓ risk: Sutrisno et al. (2018), Takaoka et al. (2011), Tsuchiya et al. (2007)

Table 1

The data presented above lead to the conclusion, that due to the limited number of studies and inconclusive results, they do not allow for the creation of uniform dietary recommendations. Due to the limited methods of treatment, which are often associated with side effects, the use of a diet in the prevention of endometriosis is a promising prospect, and worth additional research. It is therefore essential to obtain more data through more research, and it may be possible to develop dietary recommendations soon to reduce the risk of developing endometriosis.

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