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Role of bisphenol A in endometriosis

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SUMMARY

Endometriosis is a condition of heterogeneous etiology defined as the presence of endometrial tissue outside of the uterus. The disease usually affects women of child-bearing age. Currently, it is believed that there is a whole group of factors that may be responsible for endometriosis. Bisphenol A is an organic synthetic compound from the group of phenols. It affects endocrine glands, including the thyroid. It causes complex disorders in the central nervous system and directly affects the immune system and fertility. Studies show the relationship between exposure to bisphenol A and development of endometriosis. Researchers have found that higher levels of BPA in urine are associated with a higher incidence of endometriosis in the pelvic peritoneum.

Key words: bisphenol A; endometriosis; dysmenorrhea

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INTRODUCTION

Endometriosis, also called adenomyosis, is a condition of heterogeneous etiology defined as the presence of endometrial tissue outside of the uterus. Foci of endometriosis contain both glandular cells and endometrial stroma. The disease usually affects women of child-bearing age and occurs, as estimated, in approximately 10% of them. The most common symptom is dysmenorrhea. As many as 50% of women with painful menstruation suffer from endometriosis. Considering lower comfort of life, overuse of analgesics as well as absence at work and school, it can be stated that this disease constitutes a serious social problem. Infertility is its most common complication. Approximately 80% of women with fertility problems suffer from endometriosis [1].

Endometriosis is a condition of heterogeneous etiology. Currently, it is believed that there is a whole group of factors that may be responsible for its development. The exact determination of its causes seems significant taking into consideration its prevalence [1].

ETIOLOGY

Endometriosis was first described in medical texts approximately 4 thousand years ago. *Corpus Hippocreateum* depicts relatively accurate symptomatology, including infertility. In the modern era, the disease was described by Daniea Shroea in *Disputatio Inauguralis Medica Ulceribus Ulceri* from 1690. Since the 19th century, scientists have presented various theories on its origin. Investigations have yielded, e.g. Recklinghausen's theory (endometrial tissue originates from the Wolffian ducts), Thomas Cullen's theory (endometrial tissue comes from the Mullerian ducts) or cell metaplasia theory put forward by Heinrich Waldeyer. The last theory, which was developed for years, is based on the common origin of the peritoneal epithelium and endometrium from the primor-

dial body cavity (coelom). Metaplasia can be affected by environmental, infectious and hormonal factors [2,3].

In 1925, John Sampson put forward a theory about retrograde menstruation which, until today, remains the most common theory about the origin of endometriosis despite its numerous shortcomings. The Sampson's idea assumes that menstrual blood escapes through the fallopian tubes to the peritoneal cavity where endometrial debris is implanted [2,4]. However, it has been proven that retrograde menstrual flow through the fallopian tubes occurs during laparoscopy in 76–90% of healthy women, which undermines Sampson's theory [5]. Nonetheless, there are studies on animals showing that increased retrograde menstrual flow does increase the risk of endometriosis [6].

Another theory that derives from the one on cellular metaplasia states that endometriosis foci develop from cells that were left behind after Mullerian duct migration. These cells are believed to react to both estrogens and other factors that directly stimulate their conversion to endometriosis foci. These factors include genetic predisposition as well as anatomic, immunologic and environmental factors [7].

Recently, another theory has been gaining popularity. It is based on stem cells and assumes that endometriosis foci develop from progenitor endometrial cells and stem cells originating from the bone marrow. It states that cells can migrate both via the path of retrograde menstruation and via lymphatic and blood vessels, and implant in the pelvic peritoneum or other sites where such foci have been observed. This theory seems to be the most coherent and explains cases of endometriosis in the pelvis minor and in remote anatomical regions, such as the lungs or brain, in a holistic way [8]. All these theories assume increased affinity of the endometrium to implant beyond its natural location, which can be linked with elevated levels of both external estrogens and xenoestrogens [4–7].

BISPHENOL A

Xenoestrogens are a heterogeneous chemical group of compounds that can have both an aromatic and aliphatic structure. Their action is similar to the action of estrogens in animals [9]. Bisphenol A (BPA; 2,2-bis(4-hydroxyphenyl) propane) is an organic synthetic compound from the group of phenols. It was first synthesized by condensation of acetone and two equivalents of phenol by a Russian chemist, Alexander Dianin [10]. Bisphenol A is applied in the industry as a monomer used for the production of polycarbonates and epoxy resins. It is present in plastic containers of food products, cosmetics and dental fillings. High temperature and appropriate pH trigger accelerated hydrolysis of chemical bindings between BPA monomers, thus releasing bisphenol A and rendering it capable of migrating from the container to the product. Exposure takes places after ingesting foods containing BPA. Lipophilicity of bisphenol facilitates toxin penetration through the skin and its accumulation in tissues and organs [11].

BPA exerts action similar to estrogen and binds with estrogen receptors: ERá and, to a lesser degree, ERâ, as well as membrane estrogen receptor GPR 30, which makes it a xenoestrogen. Owing to its chemical structure, it easily crosses the placenta and is found in breast milk [12].

Bisphenol A affects endocrine glands, including the thyroid. The compound also binds with the androgen receptor. As a potent lipophilic substance, it may cause complex disorders in the central nervous system. Moreover, it directly affects the immune system. Research has revealed its possible adverse effects on fertility, both in the mechanisms of male and female infertility [11].

ROLE OF BISPHENOL A IN ENDOMETRIOSIS

Animal studies show the relationship between exposure to bisphenol A and development of endometriosis. Women exposed to BPA to the greater degree than the average for the population have been shown to develop endometriosis more frequently. Signorile et al. [13] attempted to determine the mechanism of endometriosis development after bisphenol A exposure in mice. For this purpose, 100 and 1,000 μg/kg was injected to mice daily from the first day of pregnancy to the seventh day after delivery. Endometriosis-like structures were found around the genital organs in the offspring. Such a finding was seen in only one case in the control group. The authors conclude their work with a suggestion that endometriosis can result from changes in the Mullerian duct development during pregnancy, which can be caused by epigenetic action of bisphenol A [13].

Simonelli et al. [14] designed a study aiming to show a relationship between BPA exposure

and the development of endometriosis in humans. This study involved the assessment of bisphenol A levels in the peritoneal fluid of patients with endometriosis and comparison of the findings with controls. Urine and peritoneal fluid samples were tested for bisphenol A levels by gas chromatography coupled to mass spectrometry (GC-MS). Detectable BPA levels were found in all analyzed urine samples with statistically significant differences between the study group and controls. Patients with endometriosis had higher bisphenol A levels in the body fluids [14].

Similar outcomes were reported by authors from the United States who evaluated BPA levels in urine and assessed laparoscopic images of the pelvis minor. They found that higher levels of BPA in urine were associated with a higher incidence of endometriosis in the pelvic peritoneum. However, a correlation between BPA concentration in urine and the occurrence of endometriosis within the ovarian tissue was not found. The authors suggest that the etiology of the disease in the ovary and pelvic peritoneum can have various backgrounds [15].

Another work that sheds some light on the etiology of endometriosis involved the assessment of periglandular fibrosis (collagen concentration) in the endometrium. It occurred that patients with higher bisphenol A levels in urine had more collagen around glands. The authors concluded that this could be conductive to increased affinity of the endometrium to implant within the peritoneum, which entails formation of endometriosis foci [16].

CONCLUSION

Endometriosis is a common disorder of unknown etiology. Research indicates a relationship between bisphenol A exposure as well as its concentration in body fluids and the occurrence of endometriosis in women. Further detailed studies are needed to specify the role of bisphenol A in the etiology of this condition. Considering the fact that endometriosis mainly affects women of child-bearing age, thereby lowering the quality of life, unambiguous, effective and minimally invasive diagnostic and therapeutic schemes must be developed.

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