

The relationship between intestinal microbiota and polycystic ovary syndrome

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PCOS- (Polycystic Ovary Syndrome) - polycystic ovary syndrome

Abstract:

Introduction: PCOS is a hyperandrogenic and low-pathogenic disease and patients suffering from PCOS have significantly lower intestinal microbiota variation in comparison with healthy individuals.

Aim of the study: The aim of the work is to overview the literary production regarding reliance between intestinal microbiota and polycystic ovary syndrome.

Conclusions: Results of the research show change in microbiome data amongst women suffering from polycystic ovary syndrome.

Streszczenie:

Wstęp: PCOS to choroba hiperandrogenowa i niski estrogenowa, a pacjenci cierpiący na PCOS mają znacznie niższe zróżnicowanie mikrobioty jelitowej w porównaniu ze zdrowymi osobami.

Cel pracy: Celem pracy jest przegląd aktualnego piśmiennictwa na temat zależności pomiędzy mikrobiotą jelitową a zespołem policystycznych jajników.

Wnioski: Wyniki badań wykazują zmianę mikrobiomu u kobiet chorujących na zespół policystycznych jajników.

Polycystic ovary syndrome

Polycystic ovary syndrome is an increasingly diagnosed cause of infertility. This disease is heterogeneous. Both genetic, hormonal and environmental factors are important in the creation of this team. There are many suggestions and evidence for an important genetic component in the etiopathogenesis of this disease. Both genetic, hormonal and environmental factors are important in the creation of this team [1,2]. Among the environmental risk factors for PCOS, obesity, which according to the World Health Organization (WHO) has increased significantly and became the most common cause of global health problems in the last twenty years, has an impact on PCOS - on the one hand it has an impact on carbohydrate metabolism, increasing insulin resistance and causing hyperinsulinaemia, and on the other hand leads to a decrease in fertility by disturbing the balance of steroid hormones in the body and results in increased symptoms of hyperandrogenisation[3,4]. Also, the increase of androgens causes further symptoms, such as: hirsutism (excessive hair growth in women), acne, seborrhea, alopecia, and in extreme cases - lowering the voice and changing the body's silhouette. Excessive hair growth can appear on the chest, face, arms, abdomen and other parts of the body. Hair loss or male pattern baldness is often noticed at the same time [5].

Etiology and pathogenesis of PCOS

It is difficult to treat PCOS due to the complex etiology and pathogenesis. The polycystic ovary syndrome is a clinically heterogeneous disorder whose aetiology from the time it was described in the 1930s is continually the subject of debate among scientists and clinicians.

The incidence among women varies, according to various sources, from 4-12%. In some studies, attention is paid to the difference in the incidence of this disease depending on the source - American or European. It is a complex hormonal and metabolic disorder [6,7]. It is considered the most frequent endocrinopathy amongst women of childbearing age. It is characterized by hyperandrogenism, in the ovaries the number of small, immature Graaf's follicles increase and ovulation does not occur. Ovaries are full of such bubbles that turn into cysts - hence the name of the disease. PCOS is a very complex disorder often associated with insulin resistance, glucose intolerance, obesity and mood disorders [8,9]. To recognize the PCOS team, two of the three basic criteria must be met. These include: 1) lack or rare occurrence of ovulation, 2) clinical and / or biochemical symptoms of hyperandrogenisation, 3) presence of polycystic ovaries in the ultrasound image - excluding other pathology, eg congenital adrenal hyperplasia, androgenic secreting tumors, Cushing's syndrome. Polycystic ovary syndrome is the most common cause (70%) of infertility associated with the lack of ovulation. Currently, there are many methods of assisted reproduction, enabling the offspring of women affected by PCOS. Numerous complications of pregnancy are also associated with PCOS syndrome, among which miscarriages are the most common. The incidence of spontaneous abortions is twice as high as in the control group, and their number is associated with elevated levels of luteinizing hormone, progesterone deficiency or abnormal endometrium. Other complications include preterm delivery, preeclampsia, diabetes and intrauterine deaths, which particularly affects the group of obese women. Therapeutic treatment in the treatment of polycystic ovarian syndrome should be adapted to the current needs and expectations of patients and to prevent distant complications of this syndrome[10-12].

Microbiota

Microbiota, in other words intestinal bacterial flora, forms a complex ecosystem in the human body, the largest activity, abundance and diversity is exhibited by the microbiota inhabiting the large intestine. It is estimated that there are from 500 to 1000 species belonging to 45 genera and 17 families of microorganisms, which constitute 80% of the dry mass of stool. At birth, consist of a variety of bacteria colonizing the digestive tract. Microbiota has a significant impact on the production and maintenance of immunological, hormonal, metabolic and digestive homeostasis.

The composition of intestinal bacterial microbiota changes under the influence of a number of different factors, such as:

- food.
- hormones,
- environment,
- type of delivery (via nature or via Caesarean section),
- taking antibiotics and medicines,
- age,
- stress,
- diseases [13] .

The influence of intestinal microflora on health has recently become an interesting area of research. The human digestive tract is settled by bacteria, bacteriophages, viruses and fungi and they are referred to as microbiota. At birth the composition of the microbiota is very poor but with age the amount of bacteria colonizing the digestive tract increases. A balanced bacterial composition is the key to maintaining impact resistance. A healthy intestinal microbiome consists of over 90% of the sensitivity within the Bacteroidetes and Firmicutes cluster. Microbiota affects the organizational state, affects the immune, hormonal, metabolic and digestive systems [14,15].

The relationship between intestinal microbiota and polycystic ovary syndrome

Most women with polycystic ovary syndrome have metabolic disorders that increase the risk of developing type 2 diabetes and heart disease. Studies show a close relationship between changes in intestinal microbiota and metabolic disorders- intestinal microbiota plays a key role in metabolic diseases and can modulate the secretion of cerebrovascular axis mediators.. Intestinal microbiome is one of the main regulators of circulating estrogens. When the process of converting estrogens into their active forms is disturbed by dysbiosis of intestinal bacterial flora there is a reduction in the amount of circulating estrogens which may contribute to the occurrence of PCOS [15,16]. Intestinal barrier disorders and endotoxemia may contribute to the clinical phenotype in some patients with PCOS [17]. Amongst women suffering from polycystic ovary syndrome there was a reduction in intestinal microbiome in comparison with healthy women: fecal microbiota profile contained a greater number of bacteria associated with the synthesis of steroid hormones, Nocardaceae and Clostridiaceae and smaller numbers of Akkermansia, Bacteroides, Lactobacillus, Clostridium. It is worth emphasizing that research

shows that hyperandrogenism may play a key role in changing the intestinal microbiome in women with PCOS. It should be mentioned that studies have shown that exposure of the female fetus to hyperandrogenism (which takes place in case of pregnant PCOS) can lead to long-term changes in the intestinal microflora [18-20].

References:

1. Jakubowski L. Genetic aspects of polycystic ovary syndrome. *Endokrynol Pol* 2005; 56: 285-93.
2. Legro RS. Polycystic ovary syndrome. Phenotype to genotype. *Endocrinol Metab Clin North Am* 2009; 28: 379-96.
3. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2010; 894: i-xii, 1-253. Pasquali R, Pelusi C, Genghini S, et al. Obesity and reproductive disorders in women. *Hum Reprod Update* 2003; 9: 359-72.
4. Pasquali R, Pelusi C, Genghini S, et al. Obesity and reproductive disorders in women. *Hum Reprod Update* 2013; 9: 359-72.
5. Szpringer E.A., Lutnicki K.R., Zych I.S.: Dermatologiczne konsekwencje hiperandrogenizmu u kobiet z zespołem policystycznych jajników oraz propozycje leczenia. *Wiad. Lek.*, 2006, 59, 11-12, 848-854
6. Knochenhauer ES, Key TJ, Kahsar-Miller M, et al. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. *J Clin Endocrinol Metab* 1998; 83: 3078–82.
7. Farah L, Lazenby AJ, Boots LR, et al. Prevalence of polycystic ovary syndrome in women seeking treatment from community electrologists. *Alabama Professional Electrology Association Study Group. J Reprod Med* 2009; 44: 870-74.
8. Saydam B.O., Yildiz B.O.: Gut-Brain Axis and Metabolism in Polycystic Ovary Syndrome. *Curr Pharm Des.* 2016; 22 (36): 5572-5587.
9. Lindheim L. i in.: Reproductive and Behavior Dysfunction Induced by Maternal Androgen Exposure and Obesity Is Likely Not Gut Microbiome-Mediated. *J Endocr Soc. X* 2018; 2 (12): 1363-1380.
10. Hamilton-Fairley D, Taylor A. Anovulation. *BMJ* 2003; 327: 546-9.
11. Carmina E, Lobo RA. Polycystic ovary syndrome (PCOS): arguably the most common endocrinopathy is associated with significant morbidity in women. *J Clin Endocrinol Metab* 2009; 84: 1897-9
12. Stankiewicz M, Norman R. Diagnosis and management of polycystic ovary syndrome: a practical guide. *Drugs* 2006; 66: 903-12.
13. Gołąb J., Jakóbisiak M., Lasek W., Stokłosa T.: *Immunologia*. Warszawa: Wydawnictwo Naukowe PWN, 2007, s. 272-273. ISBN 978-83-01-15154-6.

14. Hardina J. i.in: The gastrointestinal microbiota affects the selenium status and selenoprotein expression in mice. *J.Nutr. Biochem.* 2009;20:638-648.
15. Baker J.M., Al-Nakkash L., Herbst-Kralovetz M.M.: Estrogen–gut microbiome axis: Physiological and clinical implications. *Maturitas*, IX 2017 Volume 103, Pages 45–53
16. Charalampakis, V., Tahrani, AA, Helmy, A., Gupta, JK i Singhal, R. Zespół policystycznych jajników i przerost endometrium: przegląd roli operacji bariatrycznych w płodności samic. *Eur. J. Obstet.Gynecol. Reprod. Biol.* 2016 ; 207 : 220-226
17. Lindheim L . i in.: Alterations in Gut Microbiome Composition and Barrier Function Are Associated with Reproductive and Metabolic Defects in Women with Polycystic Ovary Syndrome (PCOS): A Pilot Study. *PLoS One.* I 2017; 12 (1): e0168390.
18. Sherman S.B., Sarsour N., Salehi M., Schroering A., Mell B., Joe B., Hill J.W.:Prenatal androgen exposure causes hypertension and gut microbiota dysbiosis. *Gut Microbes*, 2018;9(5):400-421.
19. Guo Y., Qi Y., Yang X., Zhao L., Wen S., Liu Y., Tang L .: Association between Polycystic Ovary Syndrome and Gut Microbiota. *PLoS One.* , IV 2016; 11 (4): e0153196.
20. Torres P.J. , Siakowska M. , Banaszewska B ., Pawelczyk L. , Duleba A.J. , Kelley S.T. , Thackray V.G. : Gut Microbial Diversity in Women With Polycystic Ovary Syndrome Correlates With Hyperandrogenism . *J Clin Endocrinol Metab.*, IV 2018, 1; 103 (4): 1502-1511.