

INTESTINAL MICROBIOTA IN THE POLYCYSTIC OVARY SYNDROME

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Abstract

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women of reproductive age. The etiology and pathogenesis of PCOS remain unclear, caused by several factors, mainly comprising genetic, neuroendocrine and metabolic causes. What is characteristic in PCOS is the excessive production of androgens by the ovaries. In recent years, a new concept, called "microgender", reveals a potential relationship between sex hormones and the intestinal microbiota.

Recent studies on the intestinal microbiota have thus suggested the possibility that intestinal dysbiosis may be a new theory for the emergence of PCOS. The secretion of some mediators of the brain-intestinal axis is regulated by the intestinal microbiota. It is interesting to explore the role of the intestinal microbiota in the PCOS, as androgen levels in women with PCOS are always increased. These studies indicated the bidirectional regulation of the intestinal microbiota and the endocrine system. The interaction between the intestinal microbiota and the endocrine and biochemical disorders in the PCOS remains unclear. Studies have suggested a modified composition of the intestinal microbiota of women with PCOS.

The paper presents new horizons regarding the key role of the intestinal microbiota in regulating sex hormones in both health and disease conditions. Recent research has also suggested that women with PCOS have an intestinal microbiome with fewer species than women without this condition. The use of probiotics might improve PCOS symptoms in patients by regulating the intestinal microbiome.

Keywords:

polycystic ovary syndrome, intestinal microbiota, ovarian dysfunction

Introduction

Polycystic ovary syndrome (PCOS) is characterized by androgen excess, ovulatory dysfunction, polycystic ovaries and is often accompanied by insulin resistance. It is difficult to treat PCOS because of the complex etiology and pathogenesis.

PCOS is the most common endocrine disorder in women during the reproductive period, with the prevalence of 6-10%, although it is supposed to be even higher, depending on the ethnic population and the criteria used for the diagnosis. The cause of PCOS remains unclear because of the unknown interactions between genetic factors and the environment.

The main features of PCOS are chronic anovulation with or without menstrual cycle disorders, clinical and / or biochemical hyperandrogenism and ultrasound detection of morphological polycystic ovaries. Obesity appears to play a role in the pathogenesis of

PCOS and is present in 40-70% of patients with PCOS. Insulin resistance (IR) is another feature of PCOS and is partially independent of obesity. There are many theories about what triggers PCOS, including genetic and environmental factors. One such theory, relatively new and currently being explored in the world of medical science, is the theory that an imbalance of the intestinal microbiota might trigger the development of PCOS (1),(Fig.1). Recent studies have associated changes in the intestinal microbiome composition and the barrier function with the microbiota imbalance of the stool, intestinal permeability, and inflammatory status in women with PCOS. The intestinal microbiota plays a major role in the state of health and disease, influencing the physiology, metabolism, nutrition and immune function. Several metabolic disorders are associated with PCOS, including insulin resistance, diabetes and obesity (2,3).

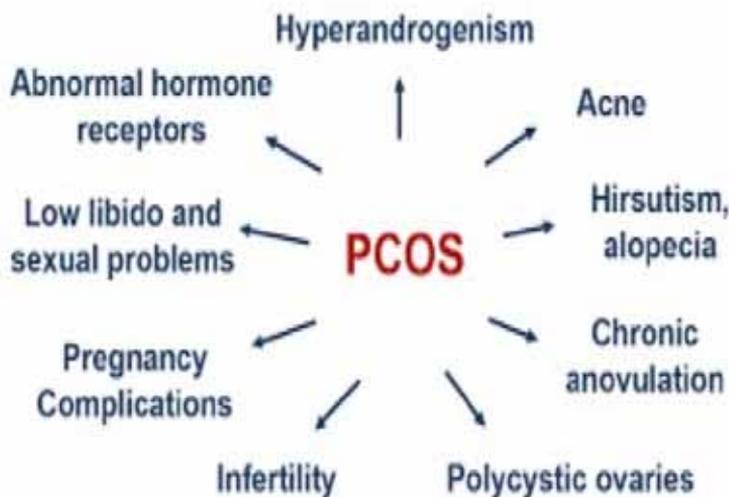


Fig. 1 Effects of polycystic ovary syndrome

(after: [https://slideplayer.com/slide/9393706/TAME THE FLAMES OF PCOS A Unique Integrative Approach](https://slideplayer.com/slide/9393706/TAME%20THE%20FLAMES%20OF%20PCOS%20A%20Unique%20Integrative%20Approach) - ppt video online download)

Polycystic ovary syndrome is an endocrine disorder, in which the excess of androgens, which among other things also affects the reproduction of 5-10% of women worldwide. Polycystic ovary syndrome leads to several complications, such as hyperandrogenism, obesity and metabolic syndrome.

The syndrome is characterized by the presence of at least two of the 3 classic features: hyperandrogenism, oligo- / anovulation and polycystic ovaries at the pelvic ultrasound. Women with PCOS, especially those with irregular menstrual cycles, may have difficulty conceiving a foetus due to anovulation. Polycystic ovary syndrome is one of the main predispositions for the onset of ovarian hyperstimulation syndrome. In addition, patients with PCOS frequently experience metabolic disorders with cardiovascular risk factors, type 2 diabetes, dyslipidaemia, visceral obesity and risk factors for the endothelial dysfunction. Therefore, PCOS is not only a problem of cosmetics and fertility, but also a major health problem that could reduce the life expectancy of women (5-7).

Like other metabolic disorders, PCOS is associated with changes in the composition of the intestinal microbiome.

Recently, a new concept has emerged, that of “microgenderomes” related to the potential roles of two-way interaction between sex hormones and the intestinal microbiota (8).

Tremellen and Pearce suggest that the intestinal microbiota dysbiosis (DOGMA) produced by a high-fat diet in patients with PCOS leads to increased intestinal permeability. Serum testosterone and androstenedione concentrations were significantly higher in patients with PCOS than in the control groups (2).

A testosterone level above 2ng / ml or 2.5 times higher than the maximum value suggests an ovarian tumour.

Excessive production of androgens and the relatively insufficient estradiol level are the essential features for patients with PCOS and very important for follicle development. Such hormonal changes in PCOS are probably associated with intestinal dysbiosis. A previous study showed that postmenopausal women with a more diverse intestinal microbiome had estrogen and estrogen metabolites in the urine (9-11).

The plasma levels of serotonin, ghrelin and peptide YY (PYY) were significantly reduced in patients with PCOS compared with controls. Intestinal dysbiosis may increase the production of androgens by the ovaries. Research has shown that 20-30% of women with PCOS have excessive adrenal androgens. Therefore, the intestinal dysbiosis, like the increase in the number of lipopolysaccharide-producing bacteria (LPS) and the decrease of protective bacteria, may be correlated with the development of metabolic disorders in PCOS. However, the relationship between the levels of serum mediators of the brain-intestinal axis and PCOS remains controversial in human studies. This study also demonstrated the association between the intestinal microbiota and the clinical parameters associated with PCOS (12-14).

One study found that women with PCOS had higher levels of certain “bad” bacterial strains in the stool sample than women without PCOS; this has shown a positive correlation with the body mass index (BMI) and the testosterone level in women with PCOS (1).

The imbalance between the “good” and “bad” bacteria in the intestine can affect ex-

acerbation and possibly the development of PCOS in several different ways. “Bad” bacteria contain what is known as lipopolysaccharide (LPS), a known stimulant of cell wall inflammation (15).

An increase in the level of insulin in the blood, as well as the increase of certain inflammatory factors, causes an increase in androgen production in the ovarian cells (2).

High levels of insulin in the blood also reduce the sex hormone binding globulin (SHBG) released from the liver, allowing the more free, bioavailable testosterone to exist throughout the body (15).

The intestinal microbiome also affects the hypothalamo-pituitary-adrenal (HPA) axis. Irregularities in this axis lead to androgen excess. In addition, many women diagnosed with PCOS suffer from increased intestinal permeability. In such a state, the tight junctions lining the wall of the intestine begin to widen. This allows larger food particles and toxins to flow into the bloodstream. This again stimulates a low-intensity, systemic inflammatory response. And this is probably why a lot of women with PCOS are also diagnosed with the “permeable” bowel syndrome. Therefore, it is reasonable that this intestinal dysbiosis has the potential to participate in the development and aggravation of PCOS. Although few or no studies have been conducted to evaluate probiotics as a treatment for PCOS, it has been shown that adjusting the balance between “good” and “bad” bacteria would improve inflammation and insulin sensitivity in general. One of the best ways to improve your gut health is to include probiotics in your diet.

A healthy diet with unprocessed foods, limited alcohol and a high amount of fibres will

help produce an environment for “good” bacteria to thrive (16).

There are various probiotic formulas available that can be extremely helpful for women with PCOS. Probiotics can help reduce the number of harmful bacteria and restore the lining of the intestine. Prebiotics favour the growth of beneficial bacteria, such as Bifidobacteria and Lactobacilli. These types of bacteria can be really important for women with PCOS because it helps to create an anti-inflammatory state in the body.

Plasma levels of serotonin, ghrelin and peptide YY (PYY) were significantly reduced in patients with PCOS compared with controls and have a significant negative correlation with waist circumference and testosterone. The study suggested a modified composition of the intestinal microbiota of women with PCOS. *Bacteroides vulgatus* was significantly increased in the intestinal microbiota of women with PCOS, and the alteration of the intestinal microbiota may be of value for the treatment of PCOS (17).

The interaction between the intestinal microbiota and the endocrine and biochemical disorders in PCOS remains unclear (18).

Tremellen and Pearce suggest that intestinal microbiota dysbiosis (IMD) (Fig.2) from a high-fat diet in patients with PCOS increases the intestinal permeability. The etiology of PCOS has two pathological aspects, including a chronic state of inflammation and insulin resistance. Both conditions are associated with IMD. IMD involves an imbalance of the intestinal microbiota, i.e., the increase in the transition of Gram-negative colonic bacteria into the systemic circulation. Therefore, a chronic inflammatory response occurs in the host.

Women who have a hormonal disorder that contributes to infertility and metabolic problems tend to have less diverse intestinal bacteria than women who do not have a hormonal disorder, according to a study published in the Endocrine Society's Journal of Clinical Endocrinology & Metabolism.

The results of the study suggest that hyperandrogenism may play an essential role in altering the intestinal microbiome in women with PCOS. Women with PCOS tend to have less diverse populations of intestinal bacteria,

a trend that seems to be linked to increased testosterone levels.

Testosterone and other androgen hormones can help shape the intestinal microbiome. Further studies are needed to investigate the primary pathophysiological mechanisms underlying the PCOS.

Further research is needed to determine whether specific intestinal bacterial species contribute to the development of PCOS and whether the microbiome offers potential pathways for treating the disease.

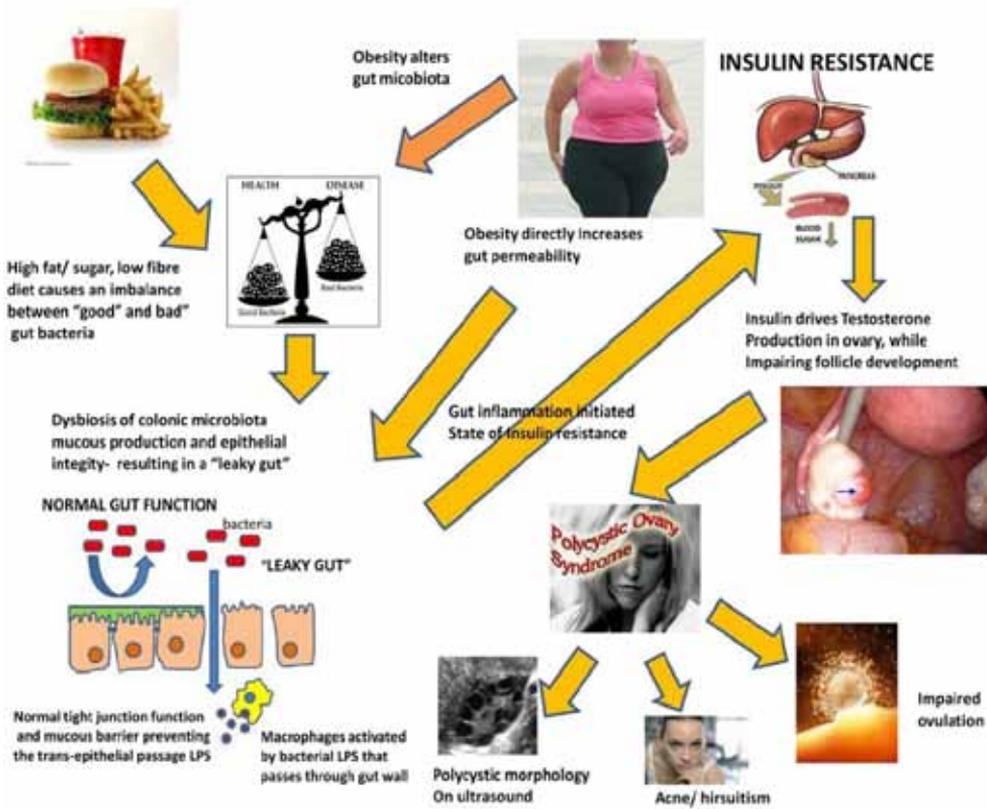


Fig. 2 Dysbiosis of gut microbiota (DOGMA)

(after: <http://www.drperlmutter.com/wp-content/uploads/2015/10/Dysbiosis-of-Gut-Microbiota-DOGMA-final-published-version.pdf>, Tremellen K)

Conclusions

Polycystic ovarian syndrome is an endocrine disorder that is diagnosed by the association between anovulation, hyperandrogenism and polycystic ovary morphology. PCOS is closely related to the intestinal microbiota. These results indicated that the dysbiosis of the intestinal microbiota is associated with PCOS pathogenesis. This paper provides the first evidence of the contribution of intestinal microbiota composition to PCOS pathogenesis. The beneficial effects of probiotic supplementation on markers for insulin metabolism and lipid profiles have been recently reported in patients with PCOS. The modulation of the intestinal microbiota may be beneficial for the treatment of PCOS.

Conflict of interest

The author has no conflict of interest to make the declaration, had full access to all the data in the study and takes responsibility for the accuracy of the data analysis.

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