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INSULIN RESISTANCE IN POLYCYSTIC OVARY SYNDROME

Abstract

PCOS has a leading place in women's infertility. Based on the data of recent researches, Anti-Mullerian hormone (AMH) has been considered as one of the diagnostic criteria for PCOS. The aim of study was to determine the interrelation of Anti-Mullerian hormone with hormonal and ovarian morphological characteristics in patients with PCOS, with and without insulin resistance. 110 women with diagnosis of PCOS were involved in the study. Patients were divided into two groups: PCOS patients with insulin resistance (60 women) and PCOS patients without insulin resistance (50 women).

All patients underwent hormonal investigation (AMH, FSH, LH, T, FT, HOMA- IR, FAI and SHBG). The volume of ovaries and the number of antral follicles (AFC) were determined by ultrasound imaging. Correlation between AMH and the ovarian hormonal and morphological characteristics has been shown. In particular, a significant positive interrelation between AMH and the volume of the ovaries in both groups was demonstrated. In the group of patients with PCOS and insulin resistance a positive interrelation between AMH and the volume of ovary, AFC was shown, as well as a negative interrelation between AMH and SHBG. In the same group a tendency of the positive interrelation between AMH and TT, HOMA-IR and IRI was seen. In the group of patients with PCOS without insulin resistence a positive interrelation between AMH and the volume of ovary was observed, as well as the tendency of positive interrelation between AMH and AFC, TT, HOMAIR, IRI. Additionally, a negative interrelation between AMH and SHBG was seen in the later patient group. Increased levels of AMH in all PCOS patients in our study, in comparison with the accepted norm, indicates on possibility of using this data in the diagnosis of PCOS. AMH levels in PCOS patients with and without insulin resistance do not differ significantly. The interrelation between AMH and the morphological characteristics of ovaries has been established.

Keywords: *hormone, insulin, polycystic ovary syndrome, endocrine, women, relationships*

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Polikistoz yumurtalıq sindromunda insulin rezistentliyi

Xülasə

Qadın sonsuzluğunun strukturunda polikistoz yumurtalıq sindromu (PYS) aparıcı mövqe tutur. Son illərdə anti-Müller hormonu PYS üçün diaqnostik meyarlardan biri hesab olunur. Tədqiqatın məqsədi insulin müqaviməti olan və olmayan polikistik yumurtalıq sindromu olan xəstələrdə anti-Müller hormon parametrləri ilə yumurtalıqların hormonal və morfoloji xüsusiyyətləri arasında korrelyasiya yaratmaq idi.

Tədqiqatda PYS diaqnozu olan 30 yaşdan kiçik 110 qadın iştirak etdi. Xəstələr iki qrupa bölündü: insulin müqaviməti olan (60 qadın) və insulin müqaviməti olmayan (50 qadın). Bütün xəstələrdə aşağıdakılar müəyyən edilmişdir: anti-Müller hormonu (AMH), luteinləşdirici hormon (LH), follikul stimullaşdırıcı hormon (FSH), ümumi testosteron (TT), sərbəst testosteron (FT), sərbəst androgen indeksi (FAI), cinsi hormonu bağlayan qlobulin (SHBG), immunoreaktiv insulin (IRI), insulin müqavimət indeksi (HOMA-IR). Yumurtalıqların həcmi və antral follikulların (AFC) sayı ultrasəs ilə müəyyən edilmişdir.

Açar sözlər: *hormon, insulin, polikistik yumurtalıq sindromu, endokrin, qadınlar, qarşılıqlı əlaqə*

Introduction

Polycystic ovary syndrome (PCOS) occurs in 5-10% of women of reproductive age, although, according to the latest data, based on the criteria of the Rotterdam Consensus, this figure was 15% [The Rotterdam ESHRE/ASRM2004;19:41–7.]. PCOS is both a medical and a significant social problem, since seeing a doctor is associated with significant financial costs and affects both a woman's health in the present and is fraught with negative medical consequences and the emergence of psycho-emotional problems in the foreseeable future. All of the above significantly impairs the quality of life of a woman. Establishing the mechanisms of the pathogenesis of PCOS, improving the methods of its diagnosis and treatment are very important, since in Georgia, as well as throughout the world, PCOS occupies a significant place in the structure of female infertility and the first place among the causes of anovulatory infertility (Azziz, Carmina, Dewailly, 2006: 91: 4237-45), and in adolescents is the main cause of menstrual dysfunction and hyperandrogenism (The Rotterdam ESHRE/ASRM2004;19:41-7). Thus, PCOS is an actual problem of gynecology and reproductive medicine. Improving the reproductive health of the population of Azerbaijan has not

only medical, but also social and, possibly, political significance, given the difficult demographic situation in the country.

PCOS has a leading place in women's infertility. Based on the data of recent researches, Anti-Mullerian hormone (AMH) has been considered as one of the diagnostic criteria for PCOS. The aim of study was to determine the interrelation of Anti-Mullerian hormone with hormonal and ovarian morphological characteristics in patients with PCOS, with and without insulin resistance.

Comparison of serum anti-Mullerian hormone (AMH) in women with polycystic ovary syndrome (PCOS) and healthy women (control group). As too study of interrelation between serum Anti-Mullerian hormone (AMH) and other hormonal parameters.

Anti-Müllerian hormone is a dimeric glycoprotein that belongs to the beta-transforming growth factor (TGF-beta). AMH is generally known for its role in male sexual differentiation at the stage of embryonic development. Later it was found that AMH performs an important function in the body of women, namely in folliculogenesis. Isolation of AMH in female embryos begins at the 25th week of pregnancy and continues until menopause (Blank, 1125:76-84). In women of reproductive age, AMH is produced in the granulosa cells of the preantral and antral follicles. The highest level of its release is found in granulosa cells of preantral and antral follicles with a diameter of 4–6 mm (Dewailly, Robin, Peigne, Decanter, Pigny, Catteau-Jonard, 2016: 22(6):709-724).

The role of AMH in folliculogenesis:

- AMH inhibits the inclusion of primordial follicles in the growth process, which protects the ovarian follicular reserve from premature depletion (Dewailly, Andersen, Balen, Broekmans, Dilaver, Fanchin, Anderson, 2014: 20(3): 370-385).
- Reduces the sensitivity of follicles to follicle-stimulating hormone (FSH) by inhibiting aromatase (Blank, 2008: 1125: 76-84; Dewailly, Robin, Peigne, Decanter, Pigny, Catteau-Jonard, 2016: 22(6): 709-724) and inhibits FSH-dependent growth of preantral follicles (Dumont, 2013: 137).
- Reduces the number of luteinizing hormone (LH) receptors in granulosa cells.

Recent studies have considered a positive interrelation between AMH and the number of antral follicles (AFC), ovarian volume and total testosterone (Homburg, Ray, Bhide, Gudi, Shah, Timms, Grayson, 2013: 28:1077-83). PCOS, characterized by multiple antral follicles in the ovaries and increased ovarian volume, should be accompanied by elevated AMH values. However, some studies have not revealed a relationship between AMH and morphological, hormonal characteristics of the ovaries in patients with PCOS, for example, between AMH and LH; estradiol (Lam, Raine-Fenning, 2006: 21:2209-15).

Noteworthy are the studies, as a result of which AMH is considered as a predictor of ovarian hyperstimulation syndrome for gonadotropins in patients with PCOS (Garg, 2016: 33(1): 15-28), as well as an indicator of the biological age of the ovaries and its reserve (Nardo, Yates, Roberts, Pemberton, Laing, 2009: 24(11): 2917-23). Establishing a relationship between AMH and hormonal and morphological characteristics in patients with PCOS and insulin resistance and without it will clarify the mechanisms of PCOS pathogenesis, which is a prerequisite for its timely and effective treatment. There are conflicting data on the effectiveness of determining and analyzing AMN parameters in patients with PCOS for diagnostic and prognostic purposes (Sir-Petermann, Maliqueo, Angel, Lara, Perez-Bravo, Recabarren, 2002: 17:2573-9). However, these data are based on a study of scarce material. Research in this direction began to be carried out only in recent years, and therefore their small number. This issue requires further study and analysis. Thus, further research and accumulation of material in this direction seems appropriate and relevant.

There is increasing evidence suggesting that PCOS affects the whole life of a woman, can begin in utero in genetically predisposed subjects, it manifests clinically at puberty, continues during the reproductive years. It can also expose patients to increased risk of cardiovascular disease, hypertension, diabetes and other metabolic complications, especially after menopause (Jones, Boon, McInnes, Maffei, Carani, Simpson, 2007: 3:414-21). During the fertile period it may cause anovulatory infertility and could be associated with increased prevalence of gestational

complications, such as miscarriage, gestational diabetes and preeclampsia (Hertig, Liere, Chabbert-Buffet, Fort, Pianos, Eychenne, et al. 2010: 203:477-9). Early diagnosis is therefore crucial by enabling close follow-up and in an attempt to reduce the risk of such complications.

It is now widely recognised that insulin resistance, manifesting above all in obese or overweight women, but often also in lean PCOS women, is one of the key to this complex disorder. It determines hyperandrogenism by acting synergically with luteinising hormone (LH) on ovarian steroidogenic enzymes and on sex hormone-binding globulin (SHBG) production by the liver (Jobe, Tyler, Magness, 2013: 61:480-7).

Etio-pathogenesis and pathophysiology. Genetic and endocrine factors, together with environmental influences. In the research of etiopathogenesis of the syndrome and in the subsequent pathophysiological expression play a role genetic and endocrine as well as environmental factors.

This hypothesis is persistent by the finding of polycystic ovaries in pre-pubertal girls (Pellatt, et al.; Fertil Steril, 2011: 96(5):1246-51; Rosenfield, 2001: 45:95-104). Studies in rhesus monkeys have demonstrated that exposure of foetuses to high levels of androgens during intrauterine life determines the onset of clinical manifestations of PCOS during adolescence. Studies in sheep have shown that an excessive androgen exposure during foetal life influences early ovarian follicular activity and it may explain the typical altered folliculogenesis shown in PCOS (19).

The aforementioned observations may suggest that exposure of the foetal hypothalamus-pituitary-ovarian axis to androgen excess may trigger a series of events that could determine PCOS onset of at puberty.

The source of intra-uterine androgens excess is unlikely to be maternal, since the foetus is protected by placental aromatase activity and by high maternal SHBG concentrations.

The expression of aromatase in the placenta of PCOS women may be diminished and this could potentially be unable to prevent foetal testosterone (T) excess in PCOS pregnancies. It has been seen that the prevalence of decreased aromatase required to carry out T excess in female fetuses was reported to be extremely rare. On the other hand, recent studies on hypertensive preeclamptic pregnancies have demonstrated a significant reduction in placental ability to synthesize oestrogens, indicating a gestational impairment of T aromatization that is more common than was previously considered.

Conclusion

Elevated levels of anti-Müllerian hormone compared with the accepted norm among patients with PCOS in this study indicate the possibility of using AMH for the diagnosis of PCOS.

- AMH values in PCOS patients with and without insulin resistance do not differ significantly from each other.
- In the group of patients with PCOS and insulin resistance, by applying logistic regression, there was a tendency for an increase in LH, TT, FT, FAI and a decrease in SHBG compared to the group of patients with PCOS and normal insulin sensitivity.
- A interrelation of AMH with the morphological characteristics of the ovaries was established using the methods of linear, logistic regression and interrelation analysis, in particular, there was a significant positive interrelation between AMH and ovarian volume in both study groups.
- In the group of PCOS patients with insulin resistance, there was a significant positive interrelation of AMH with AFC and a significant negative interrelation of AMH with SHBG. In the group of patients without insulin resistance, there is only a trend of positive interrelation of AMH with AFC and a trend of negative interrelation of AMH with SHBG.
- In both groups, a positive interrelation trend was found between AMH and total testosterone (T), as well as HOMA-IR and IRI.

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