

HORMONAL STATUS OF WOMEN OF REPRODUCTIVE AGE DEPENDING ON THE PHENOTYPE OF PCOS IN THE UZBEK POPULATION

Kamola Shukhratovna Zakhidova

Center for the Development of Advanced Training of Medical Workers,
Department of Endocrinology
Tashkent, Uzbekistan

Gulnara Nishanovna Rakhimova

Center for the Development of Advanced Training of Medical Workers,
Department of Endocrinology
Tashkent, Uzbekistan

Nigora Xayritdinovna Muminova

Center for the Development of Advanced Training of Medical Workers,
Department of Endocrinology
Tashkent, Uzbekistan

ABSTRACT

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases in women of reproductive age, with an incidence of 4 to 7% in the population. The diagnosis of PCOS requires the presence of two of the following three features: menstrual irregularity with anovulation, clinical and/or biochemical signs of hyperandrogenism, and the presence of polycystic ovaries on ultrasound.

The study included 50 patients aged 18-40 years. The diagnosis was made in accordance with the criteria of the Rotterdam Consensus. A specially developed questionnaire was used to collect anamnesis in patients with PCOS. All 50 patients with PCOS by phenotype were divided into 4 groups according to phenotypes: A - full phenotype of PCOS - 20 patients; B -anovulatory-11; C - ovulatory y - 10; D - non-androgenic phenotype in 9 patients. And 20 healthy women aged 18-40 years of reproductive age were also approved.

In the study of women with PCOS, depending on the phenotype, the following results were obtained: in groups with the phenotype A, B, D, gonadotropin LH was significantly higher compared to the "ovulatory" group C. At the same time, elevated values of LH were observed in 40% of patients, while in the "ovulatory" 2 times less. In groups A, B, D in women with PCOS, the cycles are mostly constantly anovulatory, which is confirmed by ultrasound with folliculometry. Gonadotropin data FSH was significantly lower in groups with phenotype A, B, D than in the 3rd group with phenotype C, where the ovulatory cycle was preserved.

Section A-Research paper

The results of our studies of the hormonal status in women of reproductive age in the Uzbek population with PCOS, depending on the phenotype, differ from each other, there are significant fluctuations in the levels of gonadotropic and steroid hormones, which is confirmed by the data of many studies. Based on the results of the hormonal status in 4 groups with different phenotypes in women of the reproductive period, it can be assumed that in PCOS, high levels of testosterone and free testosterone are not detected in all cases.

KEYWORDS: Polycystic ovary syndrome (PCOS), anovulatory, hyperandrogenism, ovulatory, non-androgenic.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases in women of reproductive age, with an incidence of 4 to 7% in the population [1, 3] Among the currently known etiological factors, the most important are the following: suggest that the relative or absolute excess of luteinizing hormone (LH) may be due to the primary pathology of the pituitary gland or hypothalamus, which may occur when exposed to adverse factors such as: pathology of pregnancy and childbirth in the patient's mother; the girl had infections, neuro-infections, intoxications; traumatic brain injury; psycho-emotional stress, stress [2, 4, 7].

In 2003, the diagnosis of PCOS was submitted to a special International Symposium of the joint working group of the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM), on the basis of which new criteria were formed. The diagnosis of PCOS requires the presence of two of the following three features: menstrual irregularity with anovulation, clinical and/or biochemical signs of hyperandrogenism, and the presence of polycystic ovaries on ultrasound [5, 8, 9].

Depending on the combination of diagnostic features of PCOS, approved at the Rotterdam Conference, four phenotypes of the syndrome were identified: **Phenotype A**; complete, classic which includes all the diagnostic signs of PCOS: anovulation, hyperandrogenism, polycystic ovaries;

Phenotype B; anovulatory: hyperandrogenism and anovulation in the absence of ultrasound signs of PCOS;

Phenotype C; ovulatory: hyperandrogenism and polycystic ovaries in the absence of oligomenorrhea and anovulation;

Phenotype D; non-androgenic: anovulation and polycystic ovaries without hyperandrogenism.

Purpose: to study the hormonal status of women of the reproductive period, depending on the phenotype of PCOS.

MATERIALS AND METHODS

The study included 50 patients aged 18-40 years. The diagnosis was made in accordance with the criteria of the Rotterdam Consensus (The Rotterdam PCOS consensus, 2003) [10, 11].

A specially developed questionnaire was used to collect anamnesis in patients with PCOS. All 50 patients with PCOS by phenotype were divided into 4 groups according to phenotypes: A - full phenotype of PCOS - 20 patients; B -anovulatory-11; C - ovulatory y - 10; D - non-androgenic phenotype in 9 patients. And 20 healthy women aged 18-40 years of reproductive age

were also approved. The following clinical parameters of the reproductive system were assessed: age of onset of menarche, characteristics of menstruation: their regularity, whether there was a history of pregnancy, how many of them ended in childbirth or there were complications in the development of the fetus; in case of infertility and amenorrhea: primary or secondary infertility and their limitation period; the degree of hirsutism was assessed using the Ferriman-Golway scale.

All patients underwent determination of protein and steroid hormones (LH, FSH, PRL, AMH, E2, T, sT, HOMA-IR, inhibin B, TSH, 17-OH, PG, DHEA-S) in the peripheral blood. Patients gave blood for hormones in the morning, on an empty stomach from the cubital vein, on the 2nd-4th days of the menstrual cycle and for the determination of progesterone (PG) on the 21st-23rd days of the menstrual or conditionally designated cycle. The study of the hormonal status of the patients was determined by the IHLA method.

RESULTS AND DISCUSSION

In the study of women with PCOS, depending on the phenotype, the following results were obtained: in groups with the phenotype A, B, D, gonadotropin LH was significantly higher compared to the "ovulatory" group C. At the same time, elevated values of LH were observed in 40% of patients, while in the "ovulatory" 2 times less. In groups A, B, D in women with PCOS, the cycles are mostly constantly anovulatory, which is confirmed by ultrasound with folliculometry. Gonadotropin data FSH was significantly lower in groups with phenotype A, B, D than in the 3rd group with phenotype C, where the ovulatory cycle was preserved.

Table 1. Hormonal parameters in patients of the Uzbek population with PCOS depending on the phenotype.

Indicator	Healthy	Full	Anovulatory	Ovulatory	Non-	P <
	women	Phenotyp	Phenotype B	Phenotype C	androgeni	
		e A			c	
					Phenotype	
					D	
LH, mlU/ml	$8,4 \pm 0,4$	17,3 ±	16,5 ±	8,4 ±	15,6 ±	**P>0,05
		0,4*	0,7*	0,5*	0,5*	
FSH mlU/ml	$6,2 \pm 0,3$	5,10 ±	4,5 ±	6,2 ±	4,3 ±	**P>0,05
		0,3**	0,4*	0,4**	0,4*	
AMH ng/ml	$8,4 \pm 0,3$	9,4 ±	8,5 ±	9,4 ±	6,47±	**P>0,01
		0,4**	0,4*	0,6**	0,3	
DDI HI/ 1	200.2	2562	402.4	200.4	202.1	*D 0 01
PRL µIU/ml	200,3 ±	356,3 ±	403,4±	299,4±	293,1±	*P<0,01
	14,4	42*	51,4*	42,35*	76,4*	
E2 pg/ml	132,3 ±	55,3 ±	$56,2 \pm 1,11*$	172,5±	54,1 ±	*P<0,001
	9,5	2,3*		10,4*	2,4*	
T ng/ml	0,4 ±	$5,2 \pm 0,3*$	5,1±	4,2 ±	1,2 ±	*P<0,001
	0,04		0,4*	0,3*	0,7*	

(free)T ng/ml	$2,3 \pm 0,2$	6,4 ±	6,2 ±	4,34 ±	2,24±	**P<0,05
		0,15*	0,3*	0,2*	0,3**	
17OH ng/ml	0,5±	0,6±	0,55 ±	$0,67 \pm 0,07*$	0,4 ±	*P>0,05
	0,4	0,05*	0,06*		0,07*	
Inhibin B	56,2 ±	66,4±	68,4±	64,5 ±	63,2±	**P>0,05
pg/ml	3,4	2,2**	3,2**	4,3**	5,2**	
Progesterone	56,3±	13,4 ±	16,3 ±	54,2 ±	7,2 ±	**P>0,05
(PG) nmol/l	1,3	0,2*	5,4*	5,4**	0,3*	
DHEAs	208,3±	247,2±	223,4± 17,3*	246,2±	203,4±	*P>0,05
mcg/dl	11,2	13,4*		19,4*	11,2*	
Ratio	1,34	3,12*	3,66*	1,39**	3,63**	*P<0,05
LH/FSH						**P>0,05

Inhibin B is a hormone that characterizes the follicular reserve of women, in the studied groups and in healthy people, Inhibin B was not decomposed.

These results of BPD in women with PCOS were within the normal range as in healthy women.

Estradiol in the three groups with phenotype A, B, D with PCOS was significantly lower compared to the data of the control group and the group with phenotype C.

The progesterone index on days 21-23 of the menstrual cycle was significantly lower in the three groups with phenotype A, B, D than in the 2nd group with phenotype C.

Our studies once again confirmed the increase in testosterone levels depending on the phenotype, in groups A, B, C compared with group D and control.

Progesterone levels were closer to normal in group C where ovulation occurs. The health indicators were $(56.27 \pm 1.31 \text{ nmol/l})$.

An excess of the hormone LH increases the synthesis of the male sex hormone -testosterone, and the synthesis of female sex hormones estrogen and progesterone while decreasing.

The values of 17-OH and DHEA-c in all groups do not differ from thosehealthy women, thereby eliminating hyperadrogenism adrenal genesis.

The results of our studies of the hormonal status in women of reproductive age in the Uzbek population with PCOS, depending on the phenotype, differ from each other, there are significant fluctuations in the levels of gonadotropic and steroid hormones, which is confirmed by the data of many studies.

Based on the results of the hormonal status in 4 groups with different phenotypes in women of the reproductive period, it can be assumed that in PCOS, high levels of testosterone and free testosterone are not detected in all cases.

Our studies once again confirmed the increase in testosterone levels depending on the phenotype, in groups A, B, C compared with group D and control.

Section A-Research paper

As for the data on relatively low concentrations of total testosterone in the "non-androgenic" phenotype, they, like the low values of the hirsute number and the lack of acne in this phenotype, are taken for granted and do not require special comments.

Emerging HA contributes to follicular atresia, hyperplasia of the theca stroma - cells and albuginea. In addition, the degree of GA is known to be positively correlated with the level of inhibin B, which suppresses FSH secretion.

The same results were obtained by Abasheva E.I. and co-authors (5) in 2019, the goal was to study the clinical features of PCOS phenotypes in women with normogonadotropic anovulation in reproductive age.

The study included patients with anovulatory phenotypes of PCOS. Taking into account the phenotypes of PCOS, the examined women were divided into three groups of phenotype A, B, D.

In our studies of women with PCOS, depending on the phenotype in groups with the phenotype A, B, D, gonadotropin LH was significantly higher compared to the "ovulatory" group C. At the same time, elevated LH values were observed in 40% of patients, whereas in the "ovulatory" 2 times less often. Gonadotropin data FSH was significantly lower in groups with phenotype A, B, D than in group 3 with phenotype C, where the ovulatory cycle is preserved. Atykanov A.O. and co-authors (1) 2017, with PCOS proved that women have increased secretion of LH. A sufficiently high level of LH leads to stimulation of the ovarian stroma, and this leads to ovarian and adrenal androgenization and estrogenization, manifested by an increased content of testosterone, DHEA-C, estradiol and progesterone deficiency conditions. All this leads to the formation of anovulatory menstrual cycles, followed by bleeding and the development of endometrial hyperplasia of varying degrees. Paramonova O.V. and co-authors (7) 2012, examining blood hormones, show that the basal level of LH exceeds normal values in 70% of patients, a decrease in the basal level of FSH is diagnosed in 30% of cases. The most characteristic feature of PC OS is the ratio of L Hand FSG. The LH/FSH index is normal = 1-1.5, with PCOS – LH/FSH > 2.5.

The hormone that characterizes the follicular reserve Inhibin B, and others like prolactin, AMH in women, in the study groups and in healthy ones, has not been cured.

CONCLUSION

In conclusion, I would like to note that the problem of PCOS diagnosis is still far from being solved, many issues remain open and are the subject of ongoing research.

Thus, at present, for the diagnosis of PCOS, it is most appropriate to use the diagnostic consensus adopted in Rotterdam (2003), since the diagnostic approaches reflected in it, on the one hand, include classical criteria, and on the other hand, allow identifying all possible clinical variants of PCOS.

REFERENCES

1. Atykanov A.O., Januzakov N.T., Batyrkhanov S.K. "Clinical and diagnostic characteristics of polycystic ovary syndrome in women of reproductive age". // Bulletin of the KRSU. - 2017. Volume 17. No. 7.

- 2. Durmanov A.K., Otarbayev N.K. "Anti-muller hormone as an indicator of reproductive health of women with polycystic ovary syndrome". //"Therapeutic archive".-2016-6.
- 3. Davlatov S. S., Khamdamov B. Z., & Teshaev Sh. J. (2021) Neuropathic form of diabetic foot syndrome: etiology, pathogenesis, classifications and treatment (literature review). Journal of Natural Remedies. Vol. 22, No. 1(2), P. 147-156.
- 4. Abashova E.I., Shalina M.A., Misharina E.V., Tkachenko N.N., Bulgakova O.L. "Clinical features of polycystic ovary syndrome phenotypes in women with normagonadotropic anovulation at reproductive age". // Journal. 2019."Obstetrics and women's diseases".-Volume.-68.- Issue.-3.
- 5. Bozorov, A.G., Ikhtiyarova, G.A., & Davlatov, S.S. (2020). Biochemical markers for prediction of premature labor in urogenital infections // International Journal of Pharmaceutical Research, 12, P. 4894–4897.
- 6. The Consensus Working Group on PCOS, sponsored by ESHRE Rotterdam/ASRM, revised the 2003 consensus on diagnostic criteria and long-term health risks associated with polycystic ovary syndrome (PCOS) //Hum. Reprint. 2004.- Vol. 19.- pp. 41-47.
- 7. Inoyatova, F.I., Yusupalieva, G.A., Abzalova, M.Y.A., Sultanova, L.R., Akhmedov, E.A. Features of doppler indices in chronic hepatitis with the transition to liver cirrhosis in children. International Journal of Pharmaceutical Research, 2020, 12(3), pp. 4026–4029.
- 8. Inoyatova, F.I., Yusupalieva, G.A., Begmanov, R.B., Bekimbetov, K.N., Akhralov, Sh.F. Possibilities of modern echography technologies in the diagnostics of chronic viral hepatitises in children. International Journal of Pharmaceutical Research, 2020, 12(3), pp. 4040–4043.
- 9. Paramonova O.V., Korenskaya E.G., Trofimenko A.S., Zborovskaya I.A. "Modern views on methods of diagnosis and treatment of polycystic ovary syndrome". // Journal. "Medical Almanac".-2012 No. 5.
- 10. Muzafarova S.A. "Immunological and endocrine mechanisms in the pathogenesis of ovarian hyperandrogenemia in women of reproductive age". // Abstract of the doctoral (Dsc) dissertation in medical sciences. -2019.
- 11. Shodikulova G. Z., Babamuradova Z. B. Occurrence of Clinical Options of Undifferentiated Connective Tissue Dysplasia in Uzbek Population. 2020. Issue: Issue 2, Volume:24. Pages:1347-1359.
- 12. Shamsiev A.M., Shamsiev Zh.A., Rakhmanov K.E., Davlatov S.S. Differentiated treatment tactics in surgery of liver echinococcosis. Experimental and Clinical Gastroenterology. 2020;174(5):72-77. (In Russ.) https://doi.org/10.31146/1682-8658-ecg-177-5-72-77
- 13. Malik, A., Yoshida, Y., Erkin, T., Salim, D., & Hamajima, N. (2014). Hypertension-related knowledge, practice and drug adherence among inpatients of a hospital in Samarkand, Uzbekistan. Nagoya Journal of Medical Science, 76(3-4), 255-263. Retrieved from www.scopus.com