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Expression of Serum PSA, Nesfatin-1, and AMH in Patients with Polycystic Ovary Syndrome

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ABSTRACT

Insulin resistance and hyperandrogenism are the leading causes of polycystic ovary syndrome (PCOS). Therefore, it has great significance to study the expression levels of PSA, nesfatin-1, and AMH. To provide some reference for clinical diagnosis and treatment of polycystic ovary syndrome (PCOS), the expression levels of PSA, nesfatin-1, and AMH in serum of patients with polycystic ovary syndrome (PCOS) were investigated. The experimental group consisted of 200 patients with polycystic ovary syndrome treated in Shanghai Huashan Hospital from July 2018 to July 2019. The control group consisted of 150 healthy women without pregnancy. The PSA, nesfatin-1, and AMH levels in serum were detected by chemiluminescence immunoassay (CLIA) and enzyme-linked immunosorbent assay (ELISA). The serum levels of prostate-specific antigen (PSA) and anti-Mullerian hormone (AMH) were 16.53 ± 0.67pg/ml and 10.75 ± 4.02pg/ml in the experimental group (PCOS patients), which were significantly higher than those in the control group (3.27 ± 0.43pg/ml and 5.18 ± 1.84pg/ml, respectively), while the inhibitive factors in the experimental group (1.89 ± 0.99mg/ml) were significantly higher than those in the control group (1.10 ± 0.97mg/ml). There was no significant difference in nesfatin-1. The levels of PSA and nesfatin-1, nesfatin-1, and AMH and the levels of PSA and AMH in patients with polycystic ovary syndrome were positively correlated, and the differences were statistically significant. The levels of PSA, nesfatin-1, and AMH in patients with polycystic ovary syndrome of different ages were different, and the differences were significant and negatively correlated with the age increasing. PSA, nesfatin-1, and AMH levels in patients with polycystic ovary syndrome were significantly different from those in control nonpregnant women. There was a certain correlation between the levels of PSA, nesfatin-1, and AMH, and age. The results have specific clinical reference significance for the diagnosis and treatment of patients with polycystic ovary syndrome.

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Introduction

Polycystic ovary syndrome is a disease caused by endocrine disorders in women of childbearing age (1). With the accelerated pace of life, the incidence rate of diseases has increased year by year, which has seriously disturbed people's lives (2). The main clinical manifestations are hyperandrogenemia, irregular uterine bleeding and ovarian cysts (young patients are affected by the menstrual disorder of hairy infertility, while the middle-aged and elderly patients are affected by cardiovascular diseases and diabetes mellitus), which can lead to infertility in 72 percent of patients, accompanied by insulin resistance and obesity (3, 4). It has seriously affected the lives of women of all ages. If not treated for a long time, it will seriously affect reproductive health and even general health. With the development of social medicine, people pay more and more attention to PCOS, and the clinical diagnosis and treatment methods are also constantly updated (5).

The pathogenesis of PCOS is complex. It is regulated by multiple hormones and may be affected by the environment and genes. Because of its unclear etiology, the treatment has not been cured. At present, some abnormal indexes of PCOS patients are mainly monitored and symptomatically treated in the clinic (6, 7). At present, the indexes for detecting PCOS patients are mainly three sex hormones, such as

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follicle-stimulating hormone FSH, luteinizing hormone LH and testosterone T, or counting follicles, measuring ovarian volume and endometrial thickness by ultrasound (4, 8). However, the detection methods used at this stage are affected by some factors, such as personnel monitoring level and equipment technology limitations; it is difficult to obtain accurate and standardized conclusions. For example, when using a hormone to detect PCOS patients, it is affected by the patient's menstrual period, which causes certain obstacles to the diagnosis of the disease (9).

In recent years, with the development of molecular biology, it has been found that the biochemical indicators related to POCS, mainly prostate-specific antigen PSA, overexpression of PSA can cause abnormal androgen (7). PSA is expressed in the female endometrium, ovary and breast (10). Androgen combines with its receptor to promote PSA gene expression, promote PSA production and regulate PSA level (11). In PCOS patients, it is affected by androgen the level of PSA in vivo is significantly increased, which indicates that the level of PSA can be used for the diagnosis of diseases and may become a diagnostic indicator of PCOS (12). PSA has medium sensitivity and specificity in the diagnosis of PCOS patients, and the expression of PSA is low in women. Therefore, its micro expression may still be used for clinical diagnosis. Therefore, the level of PSA can be used as an indicator for the diagnosis of PCOS (13); biochemical indicators related to POCS mainly include Most PCOS patients showing obesity and insulin resistance. The ability of insulin extraction and clearance in obese patients is reduced. Nesfatin-1 regulates insulin resistance, obesity and energy supply in PCOS patients. The content of nesfatin-1 in PCOS patients is significantly increased. Many studies have shown that nesfatin-1 is associated with the pathogenesis of PCOS (14) Anti Mullerian Hormone (AMH) is the main biochemical index related to POCS. AMH is mainly secreted by granulosa cells of the ovarian antrum, and the number of antral follicle cells is detected. More and more studies have found that the serum AMH level of PCOS patients is different from that of normal people, which is significantly higher than that of normal people. AMH is closely related to follicular growth, recruitment and development (15). AMH level is not affected by menstrual cycle, hormonal contraceptives and pregnancy, and its expression is stable, which objectively reduces the inconvenience of PCOS diagnosis (16).

There are many diagnostic indicators for PCOS (15, 16), but few studies have been done on the effect of single and combined diagnosis. In order to diagnose PCOS patients more accurately and reduce the influence of objective factors, this paper explored the diagnostic efficacy of PSA, nesfatin-1 and AMH alone combined with sex hormone in patients with PCOS, and the diagnostic efficacy of PSA, nesfatin-1 and AMH in PCOS patients.

Materials and methods

Basic data of experimental subjects

From July 2018 to July 2019, 200 patients with polycystic ovary syndrome (PCOS) in Shanghai Huashan Hospital were collected. The average age was 28.5 ± 10.1 years old, including 25 cases over 45 years old, 32 cases 41-45 years old, 44 cases 31-40 years old, 52 cases between 25-30 years old and 47 cases between 20-25 years old.

The specific details are as follows: 1 Ovarian polycystic change: B-ultrasound examination showed that at least one side of the ovary had more than 12 follicles with a diameter of 2-9 mm, and (or) ovarian volume increased more than 10 ml. those who met the two criteria were diagnosed as polycystic ovary syndrome.

In the same period, 150 cases of pregnant women without pregnancy were selected as the control group, aged 19-50 years, with an average age of 29 ± 12.1 years. Their menstruation, sex hormone and body mass index should be in the normal range. At the same time, there were no other related diseases, such as no endocrine diseases, autoimmune system diseases, hyperlipidemia, ovarian-related history, etc.; they did not take contraceptives within 3 months. Their menstrual cycle was 28 days (25-35) d.

There was no significant difference in age and weight between the two groups. At the same time, it was reported to the hospital ethics committee for approval.

Experimental methods

1. Serum collection: all experimental participants were fasting in the morning for venous blood

collection, blood volume 4-6ml (without anticoagulant), and timely detection.

2. Sample processing: after the specimens were placed at room temperature for 0.5h, centrifugation (4000rpm, 5min), serum was separated and detected in time. The samples that failed to be detected in time were stored in the refrigerator at - 80°C for use, and they need to be dissolved completely.

3. Determination of AMH: electrochemiluminescence immunoassay

The detection method of AMH is mainly using the electrochemiluminescence immune system, which has high sensitivity, and the detection range is 0.01-23ng/ml. The specific operation steps refer to the manual of the conventional kit.

4. For the determination of nesfatin-1, an enzyme-linked immunosorbent assay (ELISA) was used. Refer to the manual of the conventional kit for specific operation steps.

5. PSA determination: radioimmunoassay was used. All samples were taken and Roche E170 and e1010 electrochemiluminescence instruments were used for determination. The specific operation steps were referred to the manual of conventional kit, which was provided by Roche pharmaceutical company.

Data processing

SPSS statistical software and Excel were used for data analysis. The results of the evaluation process were expressed in the form of mean ± standard error (x ± SEM). An independent sample t-test was used to compare the numerical data between groups. $P < 0.05$ means the difference is significant, and $P < 0.01$ means the difference is extremely significant.

Results and discussion

Comparison of serum FSH, LH and T in PCOS patients and healthy controls

The serum luteinizing hormone (LH) level of the experimental group (PCOS patients) was 18.01 ± 0.26mu/l, and that of the normal group was 8.02 ± 2.65u/l, the difference was statistically significant ($P < 0.001$); the testosterone (T) level of PCOS group was 5.23 ± 0.56mu/l, which was significantly higher than that of the normal group (6.12 ± 1.05mu/l), but the difference was not statistically significant The level of follicle-stimulating hormone (FSH) in PCOS group was 2.96 ± 0.68 mmol / L, which was significantly lower than that in the normal group (0.95 ± 0.20 mmol / L), but the difference was statistically significant ($P < 0.05$) (Figure 1).

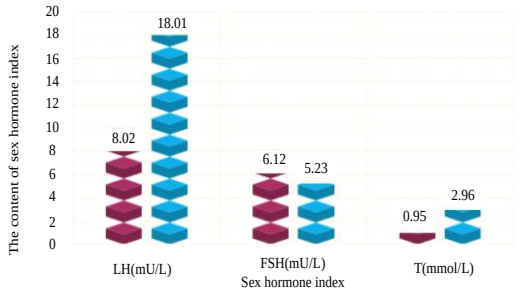

Figure 1. Comparison of FSH, LH and T in experimental group and control group (x ± s)

Comparison of serum FINS, FPG and HOMA - IR between PCOS patients and healthy controls

The serum fasting insulin (fins) level in the experimental group (PCOS patients) was 15.28±5.26mu/l, and that of the normal group was 7.32±2.14u/l, the difference was statistically significant ($P < 0.001$); the fasting blood glucose (FPG) level of the PCOS group was 5.19±0.56mmol/l, which was significantly higher than that of the normal group (4.42± 1.35mmol/l) The level of HOMA-IR in PCOS group was 4.56±1.38, which was significantly higher than that in the normal group (1.35±0.72), but the difference was statistically significant ($P < 0.001$) (Table 1 and Figure 2).

Table1. Comparison of FINS, FPG and HOMA - IR between the experimental group and the control group (x±s); group (G)

G	FINS(mU/L)	FPG(mmol/L)	HOMA-IR
CG	7.32±2.14	4.42±1.35	1.35±0.72
EG	15.28±5.26**	5.19±0.56	4.56±1.38**

*HOMA - IR=FINS(mU/L)XFPG(mmol/L)/22.5

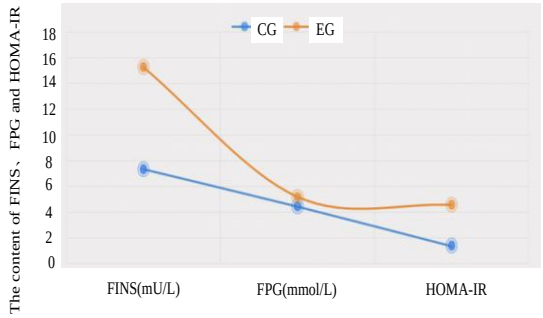

Figure 2. Comparison of FINS, FPG and HOMA - IR between the experimental group and the control group (x±s)

Comparison of serum PSA, Nesfatin-1 and AMH levels between PCOS patients and healthy controls

The serum prostate-specific antigen (PSA) level in the experimental group (PCOS patients) was 16.53±0.67pg/ml, and that of the normal group was 3.27±0.43pg/ml, the difference was statistically significant (P < 0.001); the level of nestatin-1 in PCOS group was 1.89±0.99mg/ml, which was significantly higher than that in the normal group Factor 1 (nesfatin-1 level was 1.10 ± 0.97mg/ml, but the difference was not statistically significant (P > 0.05); the level of anti-Mullerian hormone (AMH) in PCOS group was 10.75± 4.02pg/ml, which was significantly higher than that of normal group (5.18±1.84pg/ml), but the difference was statistically significant (P < 0.001), as Table 2.

Table 2. Comparison of serum PSA, Nesfatin-1 and AMH levels between PCOS patients and healthy controls (x±s); group (G)

G	PSA(pg/mL)	Nesfatin-1(mg/mL)	AMH(pg/mL)
CG	3.27±0.43	1.10±0.97	5.18±1.84
EG	16.53±0.67**	1.89±0.99	10.75±4.02**

Comparison of serum PSA, Nesfatin-1 and AMH levels in PCOS patients of different ages

Prostate-specific antigen (PSA): with the increase of age in patients with PCOS, the average value of prostate-specific antigen (PSA) increases continuously, and the growth rate of prostate-specific antigen (PSA) is about 30%. If 95% value is used as the upper limit of reference value for each age group, the reference upper limit of 20-25-year-old group is 14.98 ± 0.28pg/ml, that of 25-30-year-old group is 16.56pg/ml, and that of 31-40-year-old group is 16.56pg/ml The upper limit was 17.08pg/ml; the reference upper limit of 41-45 years old group was 18.47pg/ml; the upper limit of 45-50 years old group was 20.98 ± 0.35pg/ml.

Nesfatin-1: as the age of PCOS patients increases, the average value of nesfatin-1 increases, and the growth rate of nesfatin-1 is about 2.4%. If 95% value is taken as the upper limit of reference value for each age group, the reference upper limit of 20-25-year-old group is 1.76 ± 1.67; ng/ml, the reference upper limit of 25-30-year-old group is 1.90ng/ml; that of 31-40-year-old group is 1.90ng/ml The reference upper limit was 2.06ng/ml; the reference upper limit of 41-45 years old group was 2.18ng/ml; the upper limit of 45-50 years old group was 2.23 ± 1.85ng/ml.

Anti-Mullerian hormone (AMH): with the age of PCOS patients, the average value of anti-Mullerian hormone (AMH) continues to increase, and the growth rate of anti-Mullerian hormone (AMH) is about 29.3%. If 95% value is used as the upper limit of reference value for each age group, the reference upper limit of 20-25-year-old group is 11.88 ± 3.84ng/ml, that of 25-30-year-old group is 10.65ng/ml, and that of 31-40-year-old group is 10.65ng/ml The reference upper limit of 41-45 years old group was 6.75 ng/ml; the upper limit of 45-50 years old group was 6.03 ± 2.65 ng/ml, as Table 3.

Table 3. Comparison of serum levels of PSA, Nesfatin-1 and AMH levels in PCOS patients of different ages

Age	PSA(pg/mL)	Nesfatin-1(ng/mL)	AMH(ng/mL)
20-25	14.98±0.28	1.76±1.67	11.88±3.84
25-30	16.56±0.42	1.90±1.97	10.65±4.02
31-40	17.08±0.81	2.06±3.54	8.26±3.65
41-45	18.47±0.43	2.18±2.65	6.75±3.16
45-50	20.98±0.35	2.23±1.85	6.03±2.65

ROC curve analysis of serum PSA, Nesfatin-1, AMH and sex hormone in the diagnosis of PCOS

The ROC curve analysis of prostate-specific antigen (PSA) and sex hormone in the diagnosis of PCOS showed that the area under the curve (AUC) of prostate-specific antigen (PSA) in the diagnosis of PCOS was the largest (0.820), the sensitivity was 95.3%, the specificity was 83.5%, and the optimal cut-off point was 16.56pg/ml.

ROC curve analysis showed that the area under the curve (AUC) of nesfatin-1 in the diagnosis of PCOS was 0.761, the sensitivity was 85.3%, the specificity was 42.2%, and the best cut-off point was 2.24ng/ml.

The ROC curve analysis of anti-Mullerian hormone (AMH) and sex hormone in the diagnosis of PCOS showed that the area under the curve (AUC) of anti-Mullerian hormone (AMH) in the diagnosis of PCOS was the largest (0.854), the sensitivity was 67.3%, the specificity was 92.3%, and the best cut-off point was 6.65ng/ml.

The ROC curve analysis of follicle-stimulating hormone (FSH) and sex hormone in the diagnosis of PCOS showed that the area under the curve (AUC) of FSH in the diagnosis of PCOS was the largest (0.682),

the sensitivity was 92.4%, the specificity was 57.5%, and the best diagnostic cut-off point was 8.27iu/l.

ROC curve analysis showed that the area under the curve (AUC) of luteinizing hormone (LH) in the diagnosis of PCOS was the largest (0.765), the sensitivity was 76.3%, the specificity was 69.3%, and the best diagnostic cut-off point was 13.44 iu/l.

ROC curve analysis showed that the area under the curve (AUC) of testosterone (T) in the diagnosis of PCOS was the largest (0.769), the sensitivity was 71.8%, the specificity was 73.4%, and the best cut-off point was 0.7 IU/l. (Table 4, Table 5, and Table 6).

Table 4. Efficacy comparison of PSA and sex hormone in the diagnosis of PCOS; index (A), AUC (B), Sensitivity (C), Specificity (D), The best cut-off point of diagnosis (E)

A	B	C	D	E
PSA	0.820	95.3	83.5	16.56pg/mL
FSH	0.682	92.4	57.5	8.27IU/L
LH	0.765	76.3	69.3	13.44IU/L
T	0.769	71.8	73.4	0.7IU/L

Table 5. Efficacy comparison of Nesfatin-1 and sex hormone in the diagnosis of PCOS; index (A), AUC (B), Sensitivity (C), Specificity (D), The best cut-off point of diagnosis (E)

A	B	C	D	E
Nesfatin-1	0.761	85,3	42.2	2.24ng/mL
FSH	0.682	92.4	57.5	8.27IU/L
LH	0.765	76.3	69.3	13.44IU/L
T	0.769	71.8	73.4	0.7IU/L

Table 6. Efficacy comparison of AMH and sex hormone in the diagnosis of PCOS; index (A), AUC (B), Sensitivity (C), Specificity (D), The best cut-off point of diagnosis (E)

A	B	C	D	E
AMH	0.854	67.3	92.3	6.65ng/mL
FSH	0.682	92.4	57.5	8.27IU/L
LH	0.765	76.3	69.3	13.44IU/L
T	0.769	71.8	73.4	0.7IU/L

Diagnostic value of serum PSA, Nesfatin-1 and AMH in PCOS

The AUC of PSA diagnosis of PCOS was 0.821, 95% CI was 0.653-0.854; the AUC of nesfatin-1 diagnosis of PCOS was 0.763, 95% CI was 0.682-0.836; AUC of AMH diagnosis of PCOS was 0.753, 95% CI was 0.706-0.802; AUC of PSA + nesfatin-1 + AMH diagnosis of PCOS was 0.915, 95% CI was 0.915 The area under the curve of PSA + nesfatin-1 + AMH was significantly higher than that of PSA + nesfatin-1 + AMH (z = 4.649, 8.155, 2.917, 7.583 3 3, P < 0.05); the specificity and accuracy of combined detection of PSA, nesfatin-1 and AMH were 90.65%, 91.79% and 93.24%, respectively (Figures 3 and 4).

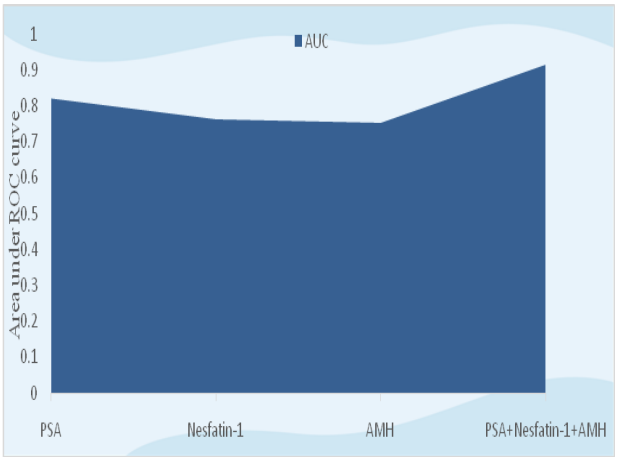

Figure 3. AUC PSA, Nesfatin-1 and AMH single detection and combined detection in the diagnosis of PCOS

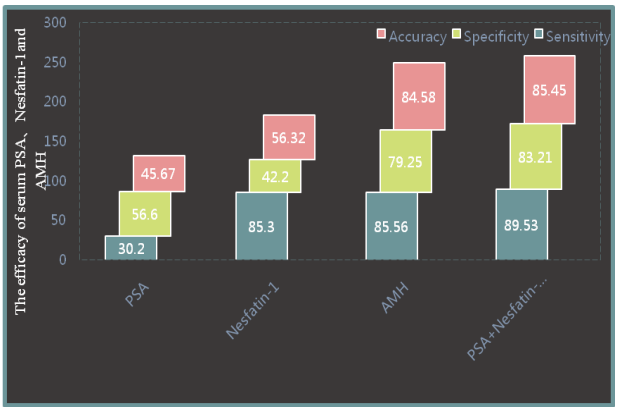

Figure 4. Diagnostic efficacy of serum PSA, Nesfatin-1and AMH in combination for PCOS

Polycystic ovary syndrome (PCOS) is an endocrine disorder, which occurs in women of gestational age. Some studies believe that the occurrence of polycystic ovary syndrome is related to genetic and environmental factors (17). At the same time, a large number of studies focus on the influence of chronic inflammation and autoimmune on polycystic ovary syndrome. As an important factor in ovarian regulation, cytokines play an important role in regulating the process from primordial follicle to primary folliculogenesis (18). This study focused on the expression of PSA, nesfatin-1 and AMH in patients with polycystic ovary syndrome and their correlation.

PSA is an important indicator of prostate cancer in men (19). In recent years, it has been found that PSA is expressed in women's ovary and endometrium, and it is further found that PSA is closely regulated by similar steroids. Some studies suggest that androgen binding to the PSA receptor can promote the expression of PSA and further regulate the level of PSA. From the results of this study, the PSA level of patients with polycystic ovary syndrome is significantly higher than that of normal people, which is consistent with the results reported in the previous literature (20, 21). At the same time, because the level of PSA in women is very low, it shows that PSA can be used as a monitoring index in the diagnosis of polycystic ovary syndrome.

AMH is a kind of transforming growth factor, its main role is to regulate early follicular recruitment. It was not detected in atresia follicles and hormone-dependent dominant follicles. Studies have found that AMH is positively correlated with the number of antral follicles and primordial follicles, and the level of AMH in patients with polycystic ovary syndrome is higher than that in healthy people. According to the results of this study, the level of AMH in patients with polycystic ovary syndrome is significantly higher than that of normal people, which is consistent with the results reported in the previous literature (22). The possible reason for this significant difference is that AMH inhibits the development of primordial follicles. At the same time, the detection of AMH is of great significance in the early screening of PCOS.

Nesfatin-1 is a neuropeptide. Some studies have shown that nesfatin-1 is involved in the occurrence and development of sex hormones and insulin resistance. That is, nesfatin-1 can affect the production and secretion of sex hormones through the hypothalamus-pituitary gonad (23). The relationship between LH, FSH and serum nesfatin-1 in patients with polycystic ovary syndrome was studied. The results showed that the level of nesfatin-1 in patients with polycystic ovary syndrome was significantly lower than that in healthy people, and there was a negative correlation between serum nesfatin-1 and sex hormones, which was consistent with the previous literature (23). This syndrome is very effective in individual, family and social life and needs to be seriously researched (24).

In conclusion, PSA, nesfatin-1 and AMH play an important role in the formation and development of the pathological mechanism of PCOS patients. Detection of serum PSA, nesfatin-1 and AMH levels in PCOS patients will help to understand the pathological causes of PCOS and guide the diagnosis and treatment of PCOS more accurately.

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None.

Interest conflict

The authors declare no conflict of interest.

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