Pakistan J. Zool., pp 1-4, 2023. **DOI**: https://dx.doi.org/10.17582/journal.pjz/20230319170342

Short Communication

Correlation of Serum Pentraxin 3, Apelin and sRAGE with Obesity and Glycolipid Metabolism in Polycystic Ovary Syndrome

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ABSTRACT

The objective of this study was to analyze the correlation of serum PTX3, apelin and sRAGE with obesity and glycolipid metabolism in polycystic ovary syndrome (PCOS). The sample of 82 PCOS patients was divided into the overweight subgroup and normal weight subgroup according to the BMI of all subjects. The morning fasting venous blood of all subjects was collected and detected by radioimmunoassay. The levels of apelin, PTX3 and sRAGE, FPG, FINS, TC, LDL-C, TG, and HDL-C were detached using enzyme-linked immunosorbent assay and HOMA was calculated -IR. Spearman was used to analyzing the correlation of PTX3, apelin and sRAGE with obesity and glycolipid metabolism in PCOS patients. PTX3 and sRAGE were decreased while the levels of apelin were raised than normal weight subgroups. The levels of PTX3 and sRAGE were reduced than those of control subgroups, and the levels of apelin were raised than those of control subgroups. The levels of FINS, FPG, HOMA-IR and WHR in obesity subgroups of each group were raised than those in normal weight subgroups of the same group; the levels of FINS, FPG and HOMA-IR in obesity subgroups of each group were raised than those in control subgroups. The levels of TG and LDL-C were higher than those of the normal weight subgroups. Spearman analysis showed that PTX3 and sRAGE were negatively correlated with FINS, FPG, HOMA-IR and BMI, and apelin was positively correlated with FINS, FPG, HOMA-IR and BMI, and negatively correlated with HDL-C. It was concluded that apelin and sRAGE in PCOS patients is related to obesity and glycolipid metabolism, which may be closely related to the progress of PCOS patients.

Article Information
Received 19 March 2023
Revised 25 April 2023
Accepted 16 May 2023
Available online 29 August 2023
(early access)

Authors' Contribution
YL, YH, and JP participated in conceiving the design of the study and collecting and reviewing the data and coordination of project. YM, YL, EP and XW participated in doing literature review, collecting the data and analysis and in preparing the manuscript. XY and LH helped in critical revision and finalizing the manuscript. All authors read, revised, and approved the final manuscript.

Key words
Polycystic ovary syndrome, Pentraxin 3, Apelin, sRAGE, Obesity, Glycolipid metabolism

Polycystic ovarian syndrome (PCOS) is a complex endocrine and metabolic abnormality commonly seen in reproductive agewomen, with clinical symptoms such as irregular menstrual cycles, infertility, hirsutism, hyperandrogenic acne, cortical overflow, masculine manifestations, polycystic ovarian changes, obesity, infertility and depression, and is the common female endocrine disorders (Layegh *et al*., 2016; Du and Cao, 2022). The prevalence of PCOS reaches about 6-7% amongreproductive age women, accounting for 28% of all obese women and 5% of non-obese women (Al-Gareeb *et al*., 2016). In recent years, with the acceleration of the pace of life, the incidence of PCOS has increased year by year (Bachelot, 2016). It has been found that the PCOS occurrenceis closely related to insulin resistance and compensatory hyperinsulinemia (Ganor-Paz *et al*., 2016). Angiotensin II receptor like receptor protein (apelin) is an endogenous carrier of the solitary G protein-coupled receptor APJ receptor, and widely distributed in many tissues and organs. Apelin has a variety of biological activities and is involved in the pathogenesis of hypertension and heart failure (Lv *et al*., 2017). Long orthopentraxin3 (PTX3) is a member of the orthopentraxin family. Under normal conditions, PTX3 is present at low levels, while it is highly expressed under infection, stress and autoimmunity (Yi and Guo, 2016). Soluble glycation end product receptor (sRAGE) is an endosomal secretory of receptor for advanced glycosylation end products (RAGE),

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0030-9923/2023/0001-0001 $ 9.00/0

which is present in the circulation and protects factors to stop and delay the development of certain diseases, such as diabetes, and atherosclerosis (Wannamethee *et al*., 2017). In addition, sRAGE is abnormally expressed in the serum of PCOS patients and may have a relationship with the PCOS occurrence (Yamaguchi *et al*., 2017). The aim of this experiment was to analyze the correlation between PTX3, apelin and sRAGE and obesity and glucolipid metabolism in PCOS patients.

Materials and methods

The observation group for this experimental study consisted eighty-two patients with PCOS admitted at the First People's Hospital between January 2019 and January 2020. Patients in both groups were eligible to join the study if they met the diagnostic criteria as revised by the European Society for Human Reproductive Medicine at its meeting in Rotterdam, the Netherlands (Zhang *et al*., 2016), namely (1) sporadic ovulation or anovulation; (2) ovarian polycystic-like changes; and (3) clinical and/or biochemical manifestations of hyperandrogenemia. The patients were all first-time patients without relevant treatment and signed an informed consent form. The following patients were excluded, (i) those with hyperprolactinemia, thyroid disease, Cushing's syndrome and other diseases that may cause hyper-sex hormoneemia; (ii) with serious dysfunction; (iii) with combined malignancy; (iv) taking drugs affecting sex hormones, blood glucose, insulin and lipid metabolism within the last month; (v) refused this experiment or terminated this experiment for other reasons. There were 82 cases in the observation group, all of whom were female, with a mean age of 26.15±5.10 years, and 82 cases in the observation group, all female, mean age was 26.24±5.15 years. According to the BMI values of all subjects, they were divided into overweight and normal weight subgroups. Forty cases were observed in the overweight subgroup, all females, mean age was 26.25±5.54 years and a mean BMI value of 24.52±0.45 kg/m^2. Forty two cases were observed in the normal weight subgroup, all females, with a mean age of 26.02±5.24 years and a mean BMI value of 22.52±0.62 kg/m^2. In the same period, 60 healthy people were selected as the control group in our hospital, all female, mean age was 26.25±5.14 years. The control overweight subgroup consisted of 29 cases, all females, mean age was 26.33±5.25 years and mean BMI was 24.42±0.25 kg/m^2. The control normal weight subgroup consisted of 31 cases, all females, with a mean age of 26.12±5.19 years and a mean BMI of 22.46±0.51 kg/m^2. General informationwas no significant difference between two groups (P>0.05).

For serum index, 5 ml of fasting venous blood was collected from PCOS patients 24 h after admission. Serum was seperated and levels of apelin were measured by radioimmunoassay, PTX3 and sRAGE by enzyme-linked immunosorbent assay. FPG, FINS, TC, and RAGE by the fully automated biochemical analyzer. TC, TG, LDL-C and HDL-C were measured using a fully automated biochemical analyzer. HDL-C levels, and HOMA-IR were analyzed [HOMA-IR=(FINS×FPG)/22.5].

The waist circumference and hip circumference were measured at the end of normal expiration by using a soft ruler with no elasticity and a minimum scale of 1 mm at the midpoint of the line connecting the lower edge of the rib arch and the upper edge of the iliac bone on the mid-axillary line around the abdomen, and horizontally around the abdomen for one week without pressing the skin, and at the maximum circumference of the hip at the level, both accurate to 5mm.

Statistical analyses were performed with Statistical Package for Social Sciences version 20. All the measurement data were expressed as (x±s) and a t-test was used for comparison between groups; the count data were expressed as (%) and the X^2 test was used. Spearman analysis was used to analyze the correlation of serum PTX3, apelin and sRAGE with obesity and glucolipid metabolism in patients with PCOS. The statistical results obtained were considered significant at P<0.05.

Results

The results for the levels of PTX3, apelin, sRAGE, FINS, FPG, HOMA-IR, WHR, TC, LDL-C,TG, and HDL-C in each group are shown in Table I. The serum PTX3 and sRAGE levels of subjects in each obese subgroup were reduced than those in the same normal weight subgroup, while the apelin levels were raised. FINS, HOMA-IR, WHR and FPG were raised in the obese subgroups than in the normal weight subgroups of the same group; meanwhile FINS, FPG and HOMA-IR were higher in the observed subgroups than in the control subgroups (P<0.05). The serum TG and LDL-C levels of subjects in each obese subgroup were raised than those in the same normal weight subgroup, and the TC and HDL-C levels were reduced than those in the same normal weight subgroup; the serum HDL-C levels of subjects in the observation subgroups were reduced than those in the control subgroups.

Table II shows the relationship between PTX3, apelin and sRAGE and obesity and glucolipid metabolism for the patients. Spearman analysis yielded that PTX3 was negatively related to FINS, FPG, HOMA-IR, and BMI (r-0.284, -0.423, -0.335, and -0.38) and positively related to HDL-C (r = 0.385); apelin was positively related to FINS, FPG, HOMA-IR, and BMI (r = 0.421, 0.418, 0.385, and 0.348) and negatively correlated with HDL-C (r = -0.384).

Table I. Serum indices for the patients in each group (x±s).

Indicators	Control group		Observation group	
	Normal weight (n=31)	Obesity (n=29)	Normal weight (n=42)	Obesity (n=40)
PTX3 (ng/L)	485.12±174.02	304.15±174.36	247.38±163.45	165.43±105.49
Apelin (pg/ml)	214.73±12.46	229.46±18.42	219.43±16.02	241.03±16.08
sRAGE (pg/ml)	1038±195.12	1009.43±94.12	1376.42±243.12	1327.46±98.12
FINS (mIU/L)	11.31±5.26	23.05±8.45	12.56±7.86	27.56±12.52
FPG (mmol/L)	5.38±0.94	5.61±0.39	5.42±0.42	6.25±0.84
HOMA-IR	2.71±1.28	5.81±2.16	3.06±1.85	7.86±4.28
WHR	0.84±0.05	0.91±0.07	0.82±0.05	0.91±0.04
TC (mmol/L)	4.49±1.02	4.21±0.52	4.68±0.95	4.35±0.65
TG (mmol/L)	0.83±0.33	1.65±0.84	1.38±0.69	1.98±1.42
LDL-C (mmol/L)	2.28±0.51	2.75±0.86	2.38±0.85	2.56±0.75
HDL-C (mmol/L)	1.41±0.31	1.21±0.25	1.62±0.51	1.03±0.28

PTX3, orthopentraxin 3

sRAGE was negatively correlated with FINS, FPG, HOMA-IR, and BMI (r = -0.351, -0.415, -0.318, -0.417), and positively related to HDL-C (r = 0.389) (Table II).

Table II. Correlation analysis of PTX3, apelin and sRAGE with the correlation between obesity and glucolipid metabolism.

Indicators	PTX3		Apelin		sRAGE	
	r	P	r	P	r	P
FINS	-0.284	0.012	0.421	<0.001	-0.351	0.004
FPG	-0.423	<0.001	0.418	0.012	-0.415	0.026
HOMA-IR	-0.335	0.003	0.385	0.035	-0.318	<0.001
HDL-C	0.385	<0.001	-0.384	0.005	0.389	0.015
BMI	-0.389	0.035	0.348	0.006	-0.417	0.002

Discussion

POCS is the common gynecological endocrine diseases, and more studies have shown that PCOS not only affects the female reproductive and gynecological endocrine system, but is often accompanied by a variety of metabolic abnormalities such asglucose disorders and hyperandrogenemia, resulting in a substantial increase in the risk of diabetes, dyslipidemia, and hypertension in the long term, seriously threatening the life and health of patients (Sivakumar *et al*., 2016). The occurrence and development of PCOS are concern to mild inflammatory response, metabolic disorders,and oxidative stress in the organism.

PTX3 is a novel inflammatory factor that is widely present in many diseases, and studies have shown that PTX3 is associated with atherosclerosis, coronary heart disease, gestational diabetes and chronic heart failure (Agilli *et al*., 2016). In addition, PTX3 deficiency is closely associated with severe residual defects, while the *PTX3* gene is closely associated with oocyte maturation and embryo quality (Krzanowski *et al*., 2017). Therefore, this experiment speculates that PTX3 may be closely associated with the development of reproductive endocrine disease PCOS. Apelin is a novel adipocytokine produced mainly by adipocytes, highly expressed mainly in cardiac, cerebral, renal and vascular endothelial cells, and low expressed in muscle, brown fat and liver, which dilates blood vessels, increases myocardial contractility, regulates water and salt balance, inhibits It can dilate blood vessels, increase myocardial contractility, regulate water and salt balance, inhibit insulin secretion and regulate immunity. It was found that apelin levels were significantly increased in adipocytes of animal models of obesity-related hyperinsulinemia, which exerted a direct regulatory effect on insulin, and this regulatory effect also exists in humans (Antushevich *et al*., 2016). In contrast, apelin miRNA expression in adipocytes in obesity with insulin resistance and hyperglycemia, along with high plasma apelin levels tract line, and apelin inhibits the increase in insulin levels induced by hyperglycemia (Abd-Elbaky *et al*., 2016). sRAGE is one of the receptors for advanced glycosylation end products (AGEs), which can promote inflammatory responses and participate in a variety of pathological processes is a soluble form of RAGE, which competitively binds the ligands of RAGE, thus blocking RAGE-ligand interactions and thus protecting cellular tissues, etc. from damage mediated by the RAGE-ligand axis (Murakami *et al*., 2018). In this experiment, the serum PTX3 and sRAGE levels of subjects in each obese subgroup were

reduced than those in the same normal weight subgroup, and apelin levels were raised than those in the same normal weight subgroup; the serum PTX3 and sRAGE levels of subjects in each observed subgroup were reduced than those in the control subgroup, and apelin levels were raised than those in the control subgroup, with significant differences ($P<0.05$). It is suggested that serum PTX3, apelin and sRAGE levels were abnormally expressed in PCOS patients, which may be related to the progression of PCOS and obesity.

To further analyze the relationship between serum PTX3, apelin, sRAGE, obesity, and glucolipid metabolism in PCOS patients, Spearman's analysis was performed to show that PTX3 and sRAGE were negatively related to FINS, FPG, HOMA-IR and BMI and positively related to HDL-C. Apelin was positively related to FINS, FPG, HOMA-IR and BMI and negatively related to HDL-C. It is suggested that PTX3, apelin and sRAGE are related to obesity and glucolipid metabolism in PCOS patients, and may be involved in the occurrence of lipid metabolism and glucose regulation abnormalities in PCOS patients.

Conclusion

PTX3, apelin and sRAGE showed abnormal expression status in the serum of PCOS patients, which correlated with the obesity and glucolipid metabolic status of patients, and may be closely related to the progression of PCOS patients.

Funding

Not applicable.

IRB approval

This study was approved by the First People's Hospital, Liangshan Yi Autonomous Prefecture, 610000, Sichuan Province, China.

Ethical approval

The study was carried out in compliance with guidelines issued by Ethical Review Board Committee of First People's Hospital, China. The official letter would be available on fair request to corresponding author.

Statement of conflict of interest

The authors have declared no conflict of interest.

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