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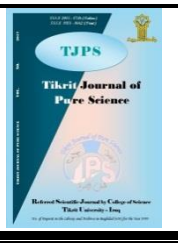

Estimation the activity of Copeptin, insulin, and C-peptide from patients with polycystic ovary syndrome

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Abstract

Copeptin, the C-terminal part of the vasopressin prohormone, is secreted stoichiometrically with vasopressin that is more easily measured than Arginine vasopressin. The present study was conducted in Kirkuk Teaching Hospital in Kirkuk city during the period from June 2016 to January 2017, to determine serum copeptin concentration in women with and without polycystic ovary syndrome (PCOS) and investigate the relationship between copeptin with insulin, and C-peptide, parameters. A total of 80 cases were enrolled in the study. All were over 18 years of age, and consisted of 40 women with POCS, and 40 healthy subjects. Blood samples were collected from all women with PCOS and healthy between 8 and 11 AM, after fasting overnight. Copeptin, insulin, and C-peptide levels in each of the cases have been measured. There was a significant increase in serum copeptin, insulin, C-peptide, and glucose levels in PCOS group when compared with healthy controls**.** So the copeptin assay may be a useful alternative method to direct measurement of Arginine vasopressin concentration.

Introduction

The polycystic ovary syndrome (PCOS) is a heterogeneous female endocrine disorder which impact 5-8% of women of reproductive age [1], and categorized by a clustering of hyperandrogenism , ovulatory dysfunction, infertility. It has lifelong implications with increased risk for metabolic syndrome, type 2 diabetes mellitus, and possibly cardiovascular disease [2].

Copeptin is a 39-aminoacid glycopeptide, which is a stable COOH-terminal part of the precursor pre-provasopressin and concealing a leucine-rich core segment, It is a neurohormon of the AVP system [3,4], that it is secreted in an equimolar ratio to AVP from hypothalamus. It is also called AVP- connected glycopeptide , and was primarily designated by Hollwerda in 1972 [5]. The AVP system has also been proposed to paticipitate to insulin resistance and DM through assortment of mechanisms including ACTH emission, glucagon motivation, and glycogenolysis [6]. Possible relations of copeptin with metabolic syndrome (MetS) , microalbuminuria ,and DM, have attracted specific attention in the current years. Thus, copeptin, as alternate marker of this system, might also be related with upset glucose homeostasis[6].

Materials and Methods

The present study was conducted in 40 healthy women the mean aged 24.33 ± 3.85years, and 40 PCOS women the mean aged 24.11 ± 4.1years. All individuals were randomly admitted into Kirkuk teaching hospital in Kirkuk city during the period from June 2016 to January 2017.

Chemicals and reagents: Specific chemicals utilized in this study are listed as below with their suppliers. Copeptin ELISA kit (Cusabio Biotech co., China), Insulin ELISA kit and C- peptide ELISA kit (Demeditec Diagnostics GmbH, Germany).

Blood samples were obtained after an overnight fasting and blood were centrifuged and stored at freeze until assayed. Copeptin levels C-peptide and insulin were measured by ELISA technique.

Inclusion criteria: 1) Oligomenorrhea or amenorrhea 2) Hyperandrogenism and / or hyperandrogenaemia [7].

Exclusion criteria: Related disorders with similar presentation like: 1. Hypothyroidism [thyroid stimulating hormone (TSH) >5 mIU/mL)], 2. Hyperprolactinaemia (serum prolactin >100 ng/mL), 3. Cushing's syndrome (cortisol > 2 µg/dL), 4. Adrenal hyperplasia and androgen secreting tumour

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(testosterone levels greater than 3 times the upper reference limit associated with relevant clinical features) [7].

Statistical Analysis: All results are presented as mean ± SD. Student t-test was used for the analysis of data. Values were considered to be significant at $P < 0.05$.

Results

The comparison of mean copeptin, insulin, and C-peptide levels of the studied groups are shown in figure 1-3. PCOS patients had a significantly higher copeptin (18.49±4.79pmol/L), insulin (52.96 ± 18.2479pmol/L), C-peptide (2.218±0.18 ng/ml) levels than control patients(12.4 ± 7.97 pmol/L), (38.39 ± 7.53pmol/L),and (1.82± 0.05ng/ml) respectively as illustrated in figure(1-3).

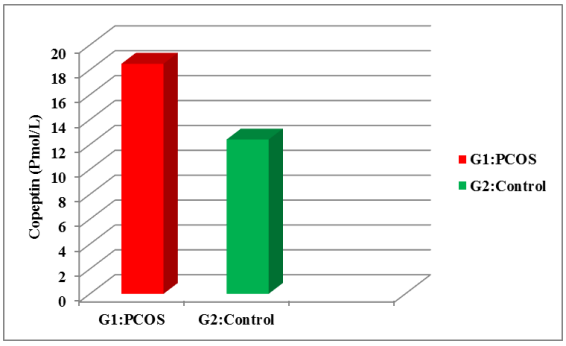

Figure 1. Serum copeptin in patients with POCS and the controls

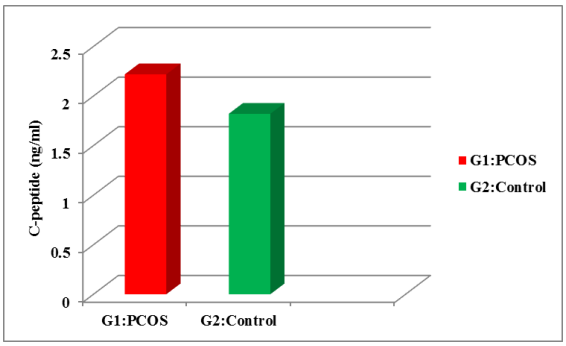

Figure 2. Serum C-peptide in patients with POCS and the controls

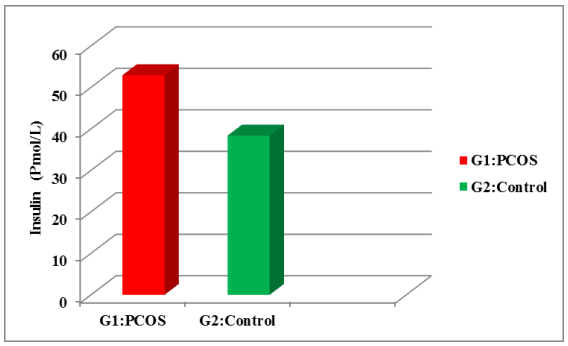

Figure 3.Serum insulin in patients with POCS and the controls.

Discussion

In present study, copeptin levels increased significantly in PCOS group as compared with control group, this finding was in accordance with Karbek et al. (2014) [7], and Taskin et al. (2015) [8] whom reported enhanced copeptin levels in PCOS women when compared with non-PCOS, may be secondary to increased hepatic triglyceride synthesis due to glucocorticoids, glucagon and epinephrine released under stress (all of which are regulated by AVP) [9].

C-peptide, initially considered an inactive molecule, has, currently, been shown to be a bioactive molecule when it binds to the surface of several cell types, and activates the calcium-dependent intracellular signalling pathway [10]. The increasing in concentration of C-peptide in patients with PCOS reflects an increase in pancreatic β-cell function [11].

Result of this study has found insulin levels are higher in serum of PCOS patients when compared with control group. Therefore, the results support previous work by Burgen et al [12].who stated that there was a correlation of hyperinsulinemia with PCOS. It has become clear that the disorder has major reproductive as well as metabolic morbidities.

In women with the polycystic ovary syndrome, hyperinsulinemia seems to reflect the hypersecretion of insulin itself, rather than of its split products. Hyperinsulinemia initiated reduction sex hormone binding globulin in hepatic, resulting in free circulating androgens which is one feature of PCOS. Cellular mechanism of insulin resistance in the POC is still argumentative , may be due to decrease binding of insulin to its receptor in blood cells and diminished lipolysis in adipocytes. While Dunaif A, [11]. using peripheral adipocytes (target cells documented for insulin action) indicated normal binding but decreased intercede glucose transport, propositioning a receptor defect.

Conclusion

Our data indicate that PCOS results in altered hormonal milieu that significant increases of serum insulin in women. Further studies with larger sample sizes are warranted to confirm these findings.

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تقدير فعالية كوبيتين، الأنسولين، و الببتيد نوع سي من المصل النساء المصابات بمتلازمة المبيض المتعدد الاكياس

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قسم العلوم الاساسية , كلية طب الاسنان ، جامعة تكريت ، تكريت ، العراق

الملخص

يعتبر الكوبتين جزء من بروهورمون فاسوبريسين، الذي يفرزيشكل متكافئ مع فاسوبريسين التي يتم قياسها بسهولة. أجريت هذه الدراسة في مستشفى كركوك التعليمي في مدينة كركوك خلال الفترة من حزيران 2016 الى كانون الثاني/يناير 2017 حيث تم قياس تركيز الكوبيتين الأنسولين والببتيد نوع سي في مصل النساء المصابات بمتلازمة المبيض المتعدد الاكياس وتحديد العلاقة الخطية بين الكوبيتين والأنسولين، والببتيد نوع سي. درسنا تركيز الكوبيتين الأنسولين، و سي– الببتيد في مصل 40 من النساء المصابات بمتلازمة تكيس المبايض ومقارنتها مع 40عينة لمجموعة السيطرة(نساء اصحاء).اظهرت النتائج زيادة كبيرة في الكوبيتين في الدم، الانسولين، الببتيد نوع سي، في النساء المصابات بمتلازمة المبيض المتعدد الاكياس بالمقارنة مع المجموعة السيطرة. أظهرت الدراسة الحالية زيادة كبيرة في مصل الأنسولين الكوبيتين، الأنسولين، والببتيد نوع سي في النساء المصابات بمتلازمة المبيض المتعدد الاكياس. قد يكون فحص الكوبيتين بديل مفيد لقياس برو–أرجينين فاسوبريسين.

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