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Evaluation the role of the hormone copeptin in patients with renal failure

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Previous experimental studies suggest that copeptin plays an important role in the development of renal failure. To measure the concentration of copeptin and some of the biochemical variables in patients with renal failure and to clarify if there is a linear relationship between them.Serum levels of copeptin and some biochemical variables were determined in 90 patients with renal failure and compared to 40 subjects as healthy control.There was a significant increase in the level of copeptin in patients with renal failure (95.22 ± 42.3 pg \ml) as compared to the control group (6.12 ± 2.07 pg\ml). In addition, the tested biochemical variables show significant increase in patients group. The results also showed that there was a significant effect of the body mass on the concentration of copeptin and that there was no significant effect of age, sex and smoking on the concentration of caffeine in the control compared to the group of patients. Copeptin serum level significantly increased in renal failure and of predictive value as variable for monitoring disease prognosis. However, large scale study is warranted to confirm this suggestion.

Keywords: Copeptin hormone, renal failure, BMI

INTRODUCTION

Chronic kidney disease (CKD) is a gradual loss of kidney function and is usually the result of complications from other serious medical condition and requires a long treatment courses (Lenford et al., 2007). Chronic renal failure has a continuous decrease in glomerular filtration rate (GFR), resulting in the accumulation of urea, creatinine and other chemicals in the blood (Guyton and Hall, 2006). The most common causes of chronic kidney disease are diabetes and hypertension and therefore there is an increasing proportion of patients with diabetic nephropathy and hypercalcemia (Lotfy et al., 2015). CKD is classified into five stages according to the level of GFR and stage 5, also called end-stage renal disease (ESRD), where the GFR level is less than (ml / min15) per 1.73 square meters and require management with transplantation or continuous dialysis (Levey et al., 2007).

The increase in uric acid is occurred in all cases and is usually considered a sign of renal dysfunction rather than a risk factor (Kuriyama et al., 2015). The high uric acid content in the blood is associated with increased risk of hypertension, chronic kidney disease, diabetic nephropathy and can be an independent risk factor for cardiovascular diseases (Keller and Blankenberg, 2009). The measurement and diagnostic use of AVP have not been used as a clinical marker for heart and kidney diseases because of the difficulty of its determination and the short plasma half-life the hormone and interaction with platelets

in the serum. While copeptin has a higher serum volume and is claimed to be more stable in the body may serve as alternative biomarker. However, simultaneous measurement of the copeptin is pivot to understanding whether increased levels of copeptin accurately reflect patients with chronic kidney disease and be stable across a full range of kidney function and renal failure in cases of kidney disease, stroke, shock, stress, hypoproteinemia, and blood volume (Katan et al., 2007). Because of their participation in the course of the hormone adrenal cortex has been proposed as a sign of high-stress reactions, including myocardial infarction and chronic renal insufficiency have obvious advantages. However, copeptin is not a specific biomarker but show increase in the early stages of the disease.

Copeptin give indications of chronic renal failure due to drop in the level of excretion (Thygesen et al., 2012) through renal system. In the past years, the copeptin hormone has been studied as both a diagnostic and predictive biomarker in various diseases such CKD and acute heart failure (Khan et al., 2007). Copeptin concentration is closely related to the concentration of argenine vasopressin in response to physiological and pathological impulses and changes in plasma level in response to changes in blood osmosis similar to argenine vasopressin excreted from the hypothalamus and are increased in response to myocardial infarction and heart failure. Studies have found that argenine vasopressin is responsible for a variety of circulatory functions, regulating vascularity and maintaining blood volume. This suggests that copeptin, which takes the carboxylic end of the argenine vasopressin, is more stable and provides alternative biologic substitutes for argenine vasopressin. Copeptin peak in the case of myocardial infarction and then decrease during the next (2-5) days (khan et al., 2007).

MATERIALS AND METHODS

Study population

The study included (90) subjects with renal failure and apparently (40) individuals as matched controls. The control group recruited from subjects referred to blood bank for blood donation with age range of 23 to 62 years and of them (22) were males and (18) were females. Patients with chronic renal failure were recruited from those attending for dialysis at Kirkuk General Hospital dialysis unit, of them 51 were males and 39 were females with age range of 17-66 years. The diagnosis of renal failure was by nephrologists according to standard criteria. Venous blood samples collected from both patients and control groups and serum separated, divided into aliquots and stored at – 20 ^{o}C until tested.

Both patients and controls divided into sub groups according to age, gender smoking, and BMI. In regard to age, group (G1) 15-30 years, G2 31-45 years and G3 46-66 years. While according to BMI, first group (16-20.9), second group (21.9-24) and third group (25-30).

Determination of serum copeptin

The serum concentration of copeptin was measured by the ELISA technique kit from (Elabscience USA) (Uysal et al, 2013) and the test performed according to the manufacturer instructions (Bhandari et al, 2009).

Determination of Urea

The method used to estimate urea is the Urease-Modified Berthelot Reaction method using diagnostic kit from Biomerieux (France) and the test performed according to manufacturer instructions (Williams et al., 1978).

Determination of creatinine

The serum concentration of creatinine was determined using the diagnostic kits from Biolabo, France, by means of color interaction (Jaffe reaction), and the reaction of the creatine with the basal pulleys (Badimon et al., 1990; Fabiny and Ertingshausen, 1996).

Statistical analysis

The findings presented as mean ± standard deviation. The data analysed using the Statistical Package for the Social Sciences (SPSS; Version 20) to determine the significance of differences between biomarkers means in patients and control groups. P value of <0.05 considered vas significant.

RESULTS AND DISCUSSION

Concentration of copeptin hormone

The results of the study showed that there was a significant ($p<0.01$) increase in the level of the copeptin in patients (95.22 ± 42.3 pg/ml) as compared to the healthy controls (6.12 ± 2.07 pg/ml), Table 1. This is in agreement with the findings of others (Esmée et al, 2017; Ponte et al., 2015). The reduced urine volume was due to reduced osmosis in patients with renal failure with subsequent increase in copeptin concentration

(Ponte et al., 2015).

Table 1:Serum concentration of copeptin in patients compared to controls

Concentrate of copeptin			
Groups	**Number**	**Mean ± SD pg/ml**	**Probability**
Control	40	6.1± 2.07	P≤0.01
Patients	90	95.22± 42.2	

This study also coincides with the study of Morgenthaler that reported an increase in copeptin in patients with CRF and follow-up stages of utilization of treatment and its interaction with kidney function in patients with chronic renal failure (Morgenthaler, 2010). Copeptin also plays an important role in the balance of water within the body by regulating excess water levels despite the fundamental role of normal physiology of the body. However, there is a growing body of evidence that copeptin has a relationship to the development of chronic renal insufficiency and high plasma levels pose a risk of decreased renal function in patients with chronic renal failure (Meijer et al., 2011).

Effect of age on copeptin hormone concentration.

The results of the study showed that there is a significant (P≤ 0.01)difference in the effect of age on the serum concentration of copeptin in patients compared to the group of controls, Table (2). This finding was in consistent with the study of Meijer et al., (2011).

The results of the study showed that there was no significant (P>0.05) difference in the serum concentration of copeptin between patients age sub groups. This is consistent with the results of Keller et al., (2010) and thus age do not influence serum concentration of copeptin, Table (2).

Effect Body Mass Index to Concentration of Copeptin Hormone

The results of the study showed that there is a significant (P≤ 0.01) difference in the effect of BMI on the level of copeptin in patients compared to that in healthy controls, Table (3). This finding agreed to that reported by Meijer et al., (2011).

The present study shows that there was a significant (P ≤ 0.01) difference in the serum level of copeptin in between patients BMI groups, Table (3).

Effect of gender on the serum concentration of copeptin hormone.

The results of this study shows that there is a significant (P≤0.01) difference in the effect of gender on the level of copeptin in patients compared to the group of healthy controls, Table (4)

The present study shows none significant (P>0.05) differences in serum copeptin between the patients male and females, Table (4). This is consistent with that reported by Enhorning et al., (2012) as gender not influence serum copeptin in patients with renal failure.

Effect of smoking on the serum concentration of copeptin hormone.

There was a significant (P ≤ 0.01) differences in serum concentrations of copeptin between patient and control groups for both smoker and non-smoker Table (5). However, smoking not shows a significant (P>0.05) influence on the concentration of serum copeptin between patient groups, Table 5. This is consistent with Keller et al., (2010) findings.

The biochemical parameters in patients with renal failure

Urea

The mean serum value of urea was significantly (P<0.01) higher in patients with renal failure (133 ± 29 mg / dl) as compared to controls (31.5 ± 7 mg / dl), Table (6). This is consistent with the findings of many studies (Janabi, 2013). The reason for this increase is that kidney failure leads to low urea excretion which contributed to accumulation of urea in blood indicating a defect in renal functions (Jassim et al., 2013).

Uric acid

The mean serum uric acid was significantly (P<0.01) higher in patients with renal failure (7.39 ± 1.9 mg / dl) as compared to controls (5.02 ± 1.2 mg / dl), Table (6). This finding is consistent with many studies (Kamal, 2014; Muslimovic et al, 2015). The presence of uric acid in the epidermis is attributed to the active cells lining the small renal tubules. Therefore, any imbalance in the kidneys function increases the concentration of serum uric acid.

Creatinine

The present study indicated that mean serum level of creatinine was significantly (P<0.01) higher in patients with renal failure (7.2 ± 1.3 mg /

dl) than in control (0.9 ± 0.26 mg / dl), Table (6). This study result is with agreement to that reported by other studies (Trivedi et al, 2016).

Table 2 :Serum copeptin concentrations in relation to age groups

Parameters	Groups	control Mean ± SD	Patients Mean ± SD	P value	P value in patients group
Copeptin (pg/ml)	G1 (15-30)	6.0 ± 2.8	98.55 ± 41.6	0.01	0.7
	G2 (31-45)	5.9 ± 1.7	90.57 ± 47.6	0.01	
	G3 (46-66)	6.4 ±2.3	99.56 ± 41.0	0.01	

Table 3 : Influence of BMI on the level of copeptin in patients and controls groups.

Parameters	Groups	control Mean ± SD	Patients Mean ± SD	Probability	Probability in patients group
Copeptin (pg/ml)	G1 (16- 20)	7.5 ± 1.4	112 ± 42.3	0.01	0.01
	G2 (21- 24)	6.8 ± 1.6	88.5 ± 39.9	0.01	
	G3 (25- 30)	5.9 ± 2.1	73.9 ± 32.1	0.01	

Table 4 : Effect of gender on the concentration of copeptin

Parameters	Groups	control Mean ± SD	Patients Mean ± SD	Probability	Probability in patients group
Copeptin (pg/ml)	Male	6.2 ± 1.9	93.8 ± 42	0.01	0.4
	Female	5.9 ± 2.3	97 ± 43.15	0.01	

Table 5 : Effect of smoking on serum concentration of copeptin

Parameters	Groups	Control Mean ± SD	Patients Mean ± SD	P value	Probability in patients group
Copeptin (pg/ml)	smokers	6.2 ± 1.9	96.5 ± 45.5	0.01	0.7
	Non-smokers	5.8 ± 2.3	93.05 ± 36.9	0.01	

Table 6:Level of biochemical in patients with renal failure and control.

Parameter	Control Mean ± SD (mg\dl)	Patient Mean ± SD (mg\dl)	P value
Urea	31.5 ± 7	133 ± 29	0.01
Uric acid	5.02 ± 1.2	7.39 ± 1.9	0.01
Creatinine	0.9 ± 0.26	7.2 ± 1.3	0.01
Sugar	82.1 ± 10.2	180.7 ± 58.2	0.01

2008).

The reason for the increase in creatinine is that it is a compound composed of metabolic processes, and in renal failure the impaired kidney function resulted in disturbance in filtration and waste disposal, leading to an increase in the quantity of creatinine. Additionally, renal failure patients have a low value for the rate of glomerular filtration rate and the concentration of creatinine is inversely proportional to it. Any reduction, even if slight, will lead to increased creatinine concentration in serum (Hsu et al,

Sugar

The mean value of blood glucose in patients with renal failure was (180.7 ± 58.2 mg / dl) whereas in the healthy control it was (82.1 ± 10.2mg / dl), with a significant difference (P<0.01), Table (6). This finding is consistent with many previously reported studies (Borai et al, 2016). The high blood sugar is due to several factors that are likely to contribute to the development of diabetes kidney disease such as frequent episodes of acute kidney injury, renal disease, hyperuricemia, and tubular cell injury. The

increased sugar levels in the later stages of renal failure increases the mortality rate of cardiovascular disease (Bora et al, 2016).

CONCLUSION

Copeptin serum level significantly increased in renal failure and of predictive value as variable for monitoring disease prognosis. However, large scale study is warranted to confirm this suggestion.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEGEMENT

The research protocol was approved by the Tikrit University College of Science Ethical Committee

AUTHOR CONTRIBUTIONS

WSK, AHA, WNH designed the experiment and wrote the manuscript. The experimental work was performed by WSK. All authors read and approved the final version.

REFERENCES

Badimon JJ, Badimon L, Fuester V, 1990. Regrression of atherosclerotic lesion by changing diet habbit. Journal Clin Invest 85:1234- 1241.

Bhandari SS, Loke I, Davies JE, Squire IB, Struck J, Ng LL, et al, 2009. Gender and renal function influence plasma levels of copeptin in healthy individuals. Clin Sci (London); 116 :257–263.

BoraiM, Borai M, Al-Zaki MM, Abdel-Azeez HA, 2016. Serum chemerin as a predictor of coronary artery disease in type 2 diabetes. International Journal of Advanced Research ;6: 1337-1343.

Enhorning S. The vasopressin system in diabetes mellitus , obesity and metabolic syndrome. Media-Tryck, Lund University, Lund, 2012; 42.

Ettema E, Heida J, Casteleijn NF, Boesten L, Westerhuis R, Gaillard CA, et al, 2017. The effect of renal function and hemodialysis treatment on plasma vasopressin and copeptin levels. 2: 410-419.

Fabiny DL, Ertingshausen G, 1996.Blood analysis. Clin Chem; 17:696-700.

Guyton AC, Hall JE, 2006. Textbook of Medical Physiology.11th Ed. Philadelphia, USA, Pennsylvania Elsevier :308-415.

Hsu CY, Ordonez JD, Chertow GM, Fan D, McCulloch CE, Go AS, 2008. The risk of acute renal failure in patients with chronic kidney disease. International Society of Nephrology; 74:101–107.

Janabi EH, 2013. Study of some biochemical parameters of hepatitis C patients and chronic renal deficiency, Master Thesis , University of Tikrit College of Science, Tikrit, Iraq.

Jassim DD, Owner AR, Aref S, 2013. A Comparative study of some liver enzymes in patients with renal failure with hepatitis C. Tikrit Pure Science J;18(5): 48-54.

Kamal A, 2014. Estimation of blood urea (BUN) and serum creatinine level in patients of renal disorder. Indian J Fundamental Appl Life Sci ;4:199-202 .

Katan M, Morgenthaler NG, Dixit KC, Rutishauser J, Brabant GE, Müller B, et al, 2007. Anterior and posterior pituitary function testing with simultaneous insulin tolerance test and a novel copeptin assay. J Clin Endocrinol Metab.;92:2640-2643.

Keller T, Blankenberg S, 2010. Copeptin improves early diagnosis of acute myocardial infarction. Circulation ;120:10-35.

Keller T, Tzikas S , Zeller T, Czyz E, Lillpopp L, Ojeda FM, et al, 2010. Copeptin Improves Early Diagnosis of Acute Myocardial Infarction. J Am Coll Cardiol; 19:2096–2106.

Khan SQ, Dhillon OS, O'Brien RJ, Struck J, Quinn PA, Morgenthaler NG, et al, 2007. C-terminal provasopressin (copeptin) as a novel and prognostic marker in acute myocardial infarction: Leicester Acute Myocardial Infarction Peptide (LAMP) study. Circulation. 115(16):2103-2110.

Kuriyama S,Maruyama Y, Nishio SH, 2015. Serum uric acid and the incidence of CKD and hypertension. Clin Exp Nephrol.;19:1127-1134.

Lenford B, Dorothy D, Jen A, 2007. Human Physiology. Boston ,USA, Free Software Foundation:186-197.

Levey AS, Atkins R, Coresh J, Cohen EP, Collins AJ, Eckardt KU, et al, 2007. Chronic kidney disease as a global public health problem: approaches and initiatives – a position statement from Kidney Disease Improving Global Outcomes. Kidney Int;72(3):247-59.

Lotfy H, Sabry S, Ghobrial, E, Abed S, 2015. The effect of regular hemodialysis on the nutritional status of children with end-stage renal disease. Saudi Journal of Kidney Diseases and Transplantation; 26(2): 263

Meijer E, BoertienWE, ZietseR, Gansevoort RT, 2011. Potential deleterious effects of vasopressin in chronic kidney disease and particularly autosomal dominant polycystic kidney disease. Kidney Blood Press Res;34:235–244.

Morgenthaler NG, 2010. Copeptin: A biomarker of cardiovascular and renal function. Congestive Heart Failure 16(4):S37-S44.

Muslimovic A, Rasic S, Tulumovic D, Hasanspahic S, Rebic D, 2015. Inflammatory markers and procoagulants in chronic renal disease stages 1-4. Medical Archives; 69:307-310.

Ponte B, Pruijm M, Ackermann D, Vuistiner P, Guessous I, Ehret G, et al, 2015. Copeptin Is Associated with Kidney Length, Renal Function, and Prevalence of Simple Cysts in a Population-Based Study 26(6); 1415-1425.

Trivedi H, Vanikar A, Patel H, Kanodia K, Kute V, Nigam L, 2016. High prevalence of chronic kidney disease in a semi-urban population of Western India. Clin Kidney J 9(3):438–43.

Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al, 2012. Third universal definition of myocardial infarction. J Am Coll Cardiol; 60(16):1581–98.

Uysal MA, Bekar N, Demirer E, Sancak M, Yılmaz V, 2013. Serum Copeptin Levels and its Relation with Other Inflammatory Markers in Acute Exacerbation of COPD. J Ann Eu Med ; 1(3): 56-61

Williams GZ, Widdowon GM, Penton J, 1978. Individual character of variation in time series studies of healthy people II, differences in values for clinical chemical analysis in serum among demographic (groups) by age and sex. Clin Chem; 24:313 -320.