

ATRIAL NATRIURETIC PEPTIDE IN METABOLIC SYNDROME OF IRAQI PATIENTS

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Article Received on 02/08/2018

Article Revised on 23/08/2018

Article Accepted on 13/09/2018

ABSTRACT

Background: Metabolic syndrome is a cluster of conditions associated with increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels, increasing risk of heart disease, stroke and diabetes. The atrial natriuretic peptides are secreted from cardiomyocytes in response to cardiac wall stress and play an important role in the regulation of blood pressure, intravascular volume, and cardiac remodeling; the natriuretic peptides also may exert a direct influence on lipid and glucose metabolism. **Objectives:** The current study aimed to investigate the role of atrial natriuretic peptide levels in metabolic syndrome of Iraqi patients. **Methods:** This study was conducted at Al-Hussein Teaching Hospital, Kerbala – Iraq from June, 2016 to Dec., 2017. One hundred twenty four patients with metabolic syndrome were included in this study. The subjects were interviewed for full history and physical examination. Diabetes was defined by either a history of fasting glucose ≥ 126 mg/dl (7.0mmol/l) or the use of insulin or hypoglycaemic medications. Serum atrial natriuretic peptide (ANP) levels were measured by ELISA kit. In addition to body mass index, lipid profiles, blood pressure, fasting glucose was measured. **Results:** The results show that there is a significant decrease in serum levels of atrial natriuretic peptide hormone in diabetic metabolic syndrome patients compared with non-diabetic metabolic syndrome patients in both sexes (P value < 0.05). **Conclusion:** We conclude that there was a significant association between lower ANP concentration and metabolic components studied. These findings raise the possibility that low level of ANP are a manifestation of metabolic syndrome, which might have pathophysiological implications.

KEYWORDS: Atrial Natriuretic Peptide hormone ANP, Metabolic Syndrome MetS, type 2 diabetes mellitus T2DM.

INTRODUCTION

Metabolic syndrome (MetS) related to insulin resistance, hyperinsulinemia, abdominal obesity, impaired glucose tolerance, dyslipidemia, hypertension and a proinflammatory and prothrombotic state had significant effects on body composition and metabolism (Lao *et al.*, 2014). These underlying mechanisms are exacerbated by the complex interplay between age, genetic conditioning, and an inappropriate lifestyle comprising sedentary lifestyle and surplus availability of energy dense salt enriched food (Fawwad *et al.*, 2015).

Type II diabetes mellitus, systolic and diastolic blood pressure levels correlates significantly with lower concentration of 25-(OH)D3 are a risk factors in diabetic patients with hypertension that leads to metabolic syndrome and then to cardiovascular diseases (Al-Tu'ma and Yosuf, 2015). Atrial natriuretic peptide is primarily stored as a propeptide in atrial granules, and is secreted and cleaved to a 28-residue mature peptide as it enters the circulation in response to atrial stretch and secreted

from cardiomyocytes in response to cardiac wall stress and play an important role in the regulation of blood pressure, intravascular volume, and cardiac remodeling (Nishikimi *et al.*, 2011 and Gruden *et al.*, 2014). The natriuretic peptides also may exert a direct influence on lipid and glucose metabolism. It has been reported that infusion of ANP elevates plasma insulin levels by 34.5% and inhibits glucagon secretion and also stimulate lipolysis and release of triacylglycerol from adipose tissue (Wang *et al.*, 2007). Reduced natriuretic peptide signaling could have detrimental effects via the promotion of lipid accumulation in adipose tissue and skeletal muscle (Bao *et al.*, 2011).

This study designed to evaluate the role of atrial natriuretic peptide level in patients with metabolic syndrome of Iraqi individuals and its association with BMI and lipid profiles.

MATERIALS AND METHODS

This study was conducted at Al-Hussein Teaching Hospital - Kerbala – Iraq from June, 2016 to Dec., 2017. One hundred twenty four patients (52 males and 72 female) with metabolic syndrome were randomly selected. The subjects were interviewed for full history and physical examination. Diabetes was defined by either a history of fasting glucose ≥ 126 mg/dl (7.0mmol/l) or the use of insulin or hypoglycaemic medications. A serum atrial natriuretic peptide level was measured by ELISA kit (Eagle Biosciences Inc., MA., USA). Blood pressure was obtained after the subject had been seated for at least 5 minutes. Systolic and diastolic pressures were measured twice, with values averaged, by the use of an automated blood pressure measurement device. Body mass index (BMI) was measured using the formula (weight in kg/height in m²) and lipid profiles were measured by various commercial kits.

Patients who suffered from, liver disease, thyroid trouble, and patients with kidney.

The studied group was divided in to two groups

1. Group I which involved diabetic patients.
2. Group II which involved non-diabetic patients.

Patients with Mets were divided into various groups depending upon the BMI, lipid profiles and BP. The age range for all samples used in this study were ranged between (35 and 65) years.

SPSS version 20 was used; independent T test was done for continuous data. The mean \pm SD. Error of all parameters measured from groups G1 and G2 were determined. P value <0.05 was considered significant.

RESULTS

Table-1- Shows the results obtained for serum Atrial natriuretic peptide (ANP) in group I (Mets with diabetes and group II (Mets without diabetes) in different age group age.

There was significant differences between two groups in (45-54) age groups (P <0.05).

Table 1: Mean \pm Std. Error values of serum (ANP) in group I (Mets with diabetes and group II (Mets without diabetes) in different age group age.

ANP (Atrial Natriuretic Peptide)			
P value	Metabolic syndrome Without Diabetic Mean \pm SE	Metabolic syndrome with Diabetic Mean \pm SE	AGE group
Non S.	55.81 \pm 5.86	37.79 \pm 3.75	35-44 year, N = 32
P <0.05	48.93 \pm 3.82	*38.54 \pm 2.73	45-54 year, N = 56
Non S.	45.4 \pm 7	40.41 \pm 3.16	55-65 year, N = 37
Non S.	50.12 \pm 2.8	*39.09 \pm 1.8	Total, N = 124

*P vale <0.05 was significant.

Table-2- Shows the results obtained for serum Atrial natriuretic peptide (ANP) in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group in duration of disease.

There was significant differences between two groups in groups with more than one year duration (P <0.05).

Table 2: Mean \pm Std. Error values of serum (ANP) in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group in duration of disease.

ANP (Atrial Natriuretic Peptide)			
P value	Metabolic syndrome Without Diabetic Mean \pm SE	Metabolic syndrome with Diabetic Mean \pm SE	Duration of disease
Non S	55.71 \pm 4.85	33.35 \pm 2.63	< 1 year
P <0.05	46.2 \pm 4.4	*43.46 \pm 2.64	1-5 years
P <0.05	51.6 \pm 5.59	*36.64 \pm 3.83	> 5 years
P <0.05	50.12 \pm 2.8	*39.09 \pm 1.8	Total

*P vale <0.05 was significant.

Table-3- Shows the results obtained for serum Atrial natriuretic peptide (ANP) in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group with different BMI groups.

There was significant differences between two groups in BMI groups with more than 30 Kg/m² and less tha 25 Kg/m² (P <0.05).

Table 3: Mean ± Std. Error values of serum (ANP) in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group in body mass index.

P value	ANP (Atrial Natriuretic Peptide)		
	Metabolic syndrome Without Diabetic Mean ±SE	Metabolic syndrome with Diabetic Mean ±SE	BMI
P<0.05	65.63 ± 2.65	*45.74 ± 4.49	< 25 Kg/m ²
Non S	54.65 ± 4.2	38.06 ± 2.7	25-30 Kg/m ²
P<0.05	41.23 ± 4.29	*36.28 ± 2.48	> 30 Kg/m ²
P<0.05	50.12 ± 2.8	*39.09 ± 1.8	Total

*P vale <0.05 was significant.

Table 4 Shows the results obtained for serum Atrial natriuretic peptide (ANP) and fasting serum glucose in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group in both male and female.

There was significant differences between two groups in both ANP and FBS in male group (P<0.05) and female group (P<0.05) and insignificant difference between male and female in each group (p>0.05).

Table 4: Mean ± Std. Error values of serum (ANP) and fasting serum glucose in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group in both male and female groups.

P value	Metabolic syndrome Without Diabetic Mean ± SE	Metabolic syndrome with Diabetic Mean ± SE	Gender	Parameters
P<0.05	47.6 ± 4.2	39.7 ± 3.2	Male (72)	ANP
P<0.05	52.4 ± 3.94	38.68 ± 2.16	Female (52)	
P<0.05	101.68 ± 4.12	268.9 ± 15.5	Male (72)	FBS
P<0.05	102.6 ± 3.2	250.47 ± 12.06	Female (52)	

ANP =Atrial Natriuretic Peptide, FBS= fasting blood sugar, mean ± Std. Error.

*P vale <0.05 was significant.

Table 5.Shows the results obtained for systolic blood pressure, diastolic blood pressure and body mass index in diabetes mellitus in metabolic syndrome group compared with individuals of non-diabetic metabolic syndrome patients group in gender at (p < 0.05).

There was insignificant differences between two groups in systolic, diastolic and BMI in male and female group (P>0.05).

Table 5: Mean ± Std. Error values for systolic blood pressure, diastolic blood pressure and body mass index in metabolic syndrome with diabetes mellitus compared with individuals of non-diabetic metabolic syndrome patients group.

P value	Metabolic syndrome Without Diabetic Mean ±SE	Metabolic syndrome with Diabetic Mean ±SE	Gender	Parameters
p>0.05	150.4 ± 3.52	144.6 ± 2.9	Male (72)	SBS
p>0.05	156.4 ± 4.9	143.8 ± 2.4	Female (52)	
p>0.05	93 ± 1.65	90.5 ± 1.34	Male (72)	DBS
p>0.05	93.6 ± 3.13	89.3 ± 1.16	Female (52)	
p>0.05	31.12 ± 1.24	29.5 ± 0.98	Male (72)	BMI
p>0.05	30.2 ± 1.05		Female (52)	

BMI =body mass index, SBS =systolic blood pressure, DBS =diastolic blood pressure, mean ± Std. Error

DISCUSSION

The observed data indicated that serum Atrial natriuretic peptide deficiency or insufficiency status was associated with an increased risk of diabetes mellitus in metabolic syndrome patients compared with individuals of non-diabetic metabolic syndrome patients. Also result show lower level in serum ANP inpatient's male diabetes mellitus in metabolic syndrome compared with

individual's male of non-diabetic metabolic syndrome patients.

ANP levels were decreased in patients with diabetes mellitus group regarding duration of disease, age and body mass index .Serum ANP levels were lower in patients who were overweight / obese or associated with hypertension and diabetic when compared with individuals of non-diabetic metabolic syndrome patient's serum ANP deficiency is associated with major effects

on the hypertension. This could potentially influence the risk of diabetes and we can explain by role Atrial natriuretic peptide function. The ANP influence SNS activity and the renin–angiotensin system. ANP and BNP are apparently antagonists to vasopressin, and the renin–vasopressin–aldosterone system so level serum ANP reduce with elevated blood pressure (hypertension). (Lafon *et al.*, 2005) low natriuretic peptide levels could predispose to insulin resistance. Reduced natriuretic peptide activity leads to greater activation of the renin-angiotensin system. Activation of the renin-angiotensin system promotes the development of insulin resistance via multiple mechanisms, including inhibition of intracellular insulin signaling, enhanced oxidative stress, inflammation, reduced adipocyte differentiation, and decreased perfusion to the skeletal muscle and pancreas (Wang *et al.*, 2007). Natriuretic peptides play role in reduce blood pressure, natriuresis and diuresis and, moreover, have powerful lipolytic and lipomobilizing activity in humans At least two adipocyte lipases are important for controlling lipolysis, hormone-sensitive lipase and adipocyte triglyceride lipase, (Wang *et al.*, 2013) The natriuretic peptides also have anti-inflammatory properties, reducing the production of tumor necrosis factor-cyclooxygenase and monocyte chemoattractant protein An association between natriuretic peptides and levels of the insulin-sensitizing hormone adiponectin has been reported, with low levels of BNP associated with low levels of adiponectin despite adjustment for body mass index Increased postprandial insulin with unchanged systemic and muscular glucose is consistent with an ANP-induced state of insulin resistance favoring lipid rather than glucose utilization (Wang *et al.*, 2007). Many studies refers to low level of ANP induce insulin resistance, and reduced natriuretic peptide activity leads to greater activation of the renin-angiotensin system. Activation of the renin-angiotensin system promotes the development of insulin resistance via multiple mechanisms, including inhibition of intracellular insulin signaling ANP is a regulator of BP-active peptides (Saito, 2010). ANP is mainly synthesized by atrial myocytes and released by relaxing blood vessels, where it acts by reducing peripheral resistance, increasing the glomerular filtration rate, inhibiting renin release and causing significant increases in urinary sodium excretion and urine output; this mechanism is involved in the regulation of BP (Potter, 2011).

CONCLUSION

We conclude that there was a connection between lower ANP concentration and metabolic components. These findings raise the possibility that low level of ANP is a manifestation of metabolic syndrome, which might have pathophysiological implications.

REFERENCES

1. Al-Tu'ma, F.J. and Yosuf, L.M.Z. (Winter) Vitamin D deficiency and hypertension in type 2 diabetic

- Iraqi patients. *J Contemp Med Sci.*, 2015; 1(1): 17–20.
2. Bao, Y.; Shang, X.; Zhou, L.; Hu,R.; Yiming Li, Y. and Ding, W. Relationship between N-terminal pro-B-type natriuretic peptide levels and metabolic syndrome.*Arch Med Sci.*, 2011; 7(2): 247-256.
3. Fawwad, A.; Siddiqui, IA.; Zeeshan, NF.; Shahid, SM. and Basit A. Association of SNP rs9939609 in FTO gene with metabolic syndrome in type 2 diabetic subjects, recruited from a tertiary care unit of Karachi, Pakistan. *Pak J Med Sci.*, 2015; 31(1): 140-145.
4. Lafontan, M.; Moro, C.; Sengenec,C.; Galitzky, J. Crampes, F. and Berlan, M. An Unsuspected Metabolic Role for Atrial Natriuretic Peptides: The Control of Lipolysis, Lipid Mobilization, and Systemic Nonesterified Fatty Acids Levels in Humans *Arterioscler Thromb Vasc Biol.*, 2005; 25: 2032- 42.
5. Lao, XQ.; Ma, WJ.; Sobko,T.; Zhang, YH.; Xu, Y.; Xu,XJ.; Dong Mei Yu, DM.; Nie, SP.; Cai, QM.; Wei, XL.; Xia,L. and Wong, MC. Dramatic escalation in metabolic syndrome and cardiovascular risk in a Chinese population experiencing rapid economic development. *BMC Public Health*, 2014; 14: 983.
6. Nishikimi, T.; Kuwahara, K. and Nakao, K. Current biochemistry, molecular biology, and clinical relevance of natriuretic peptides. *J Cardiol*, 2011; 57: 131–140.
7. Potter L. R. Natriuretic peptide metabolism, clearance and degradation *FEBS Journal*, 2011; 278: 1808–1817.
8. Saito, Y. Roles of atrial natriuretic peptide and its therapeutic use *Journal of Cardiology*, 2010; 56: 262—270.
9. Siyad, A.R. Hypertension, *H.J.D. Med.*, 2011; 3(1): 1-16.
10. Wang, T. J.; Martin, G. M.D.; Larson, S.; Michelle, J. and Keyes, M.A. Association of Plasma Natriuretic Peptide Levels With Metabolic Risk Factors in Ambulatory Individuals. *Circulation*, 2007; 20: 1346-1351.
11. Wang, T. J.; Martin, G. M.D.; Larson, S.; Michelle, J. and Keyes, M.A. Association of Plasma Natriuretic Peptide Levels With Metabolic Risk Factors in Ambulatory Individuals. *Circulation*, 2007; 20: 1346-1351.
12. Wang, J.; Lee, C.; Hsieh, J.; Chen, Y. and Hsu, B. Inverse association of long-acting natriuretic peptide with metabolic syndrome in congestive heart failure patients. *Diabetology& Metabolic Syndrome*, 2013; 5(19).