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Evaluation of Atrial natriuretic peptide and some biochemical variables in Patients with Atherosclerosis associated with Hypertension

Hawazen Fawzi Alwan Aljubouri , Wasan Nazhan Hussein Al Assi
University of Tikrit, College of Education for pure Sciences , Department of chemistry
Hawazin.f.eulwan@st.tu.edu.iq , drwasannzhan@tu.edu.iq

Abstract

The study included the evaluation of Atrial natriuretic peptide, Interlukin-6 and Electrolytes in patients with Atherosclerosis associated with Hypertension. The current study included the collection of 60 blood samples from Patients with Atherosclerosis associated with Hypertension whose ages ranged between (40-83) years. From Al-Tawfiq Al-Ahly Hospital in the City of Tikrit and private laboratories , the samples were divided into two groups: The first group (G1) which included 60 samples from Atherosclerosis associated with Hypertension and 30 samples of healthy people as a control group (C).

-The study included estimation of the levels of (Interlukin-6 ، Atrial natriuretic peptide ،Sodium ,Potassium, Chloride) for the samples under study. The results obtained from the current study: - The IL-6 level significantly elevated ($P\leq0.05$) in the serum of patients compared to the healthy people. Also-The level Atrial natriuretic peptide ، significantly decrease ($P\leq0.05$) in the serum of patients compared to the control group. as well as The level of Sodium significantly decrease ($P\leq0.05$) in serum of group patients compared to control group. also the level of potassium and chloride significantly elevated ($P\leq0.05$) in serum of group patients compared to control group

Key words / Atherosclerosis**,** Interleukin -6**,** Atrial natriuretic peptide **,** Electrolytes**.**

تقدير مستوى الببتيد الاذيني المدرر للصوديوم وبعض المتغيرات الكيموحيوية لدى المصابين بتصلب الشرايين المرتبط بارتفاع ضغط الدم

هوازن فوزي علوان الجبوري ، وسن نزهان حسين العيسى
جامعة تكريت ، كلية التربية للعلوم الصرفة ، قسم الكيمياء

مستخلص

أجريت الدراسة على 60 عينة من المرضى المصابين بتصلب الشرايين والمصاحب لارتفاع ضغط الدم، تراوحت أعمارهم بين (40–83) سنة ، اما الاصحاء فقد تم جمع 30 عينة دم وتراوحت اعمارهم بين (40–77) سنة.

تتضمن الدراسة تقدير انترلوكين 6، الببتيد الاذيني المدر للصوديوم ، وبعض الالكتروليتات والتي تشمل (الصوديوم ، البوتاسيوم ، الكلور) في مصل دم العينات قيد الدراسة. اظهرت النتائج ارتفاع مستوى انترلوكين 6 معنويا ($P\leq0.05$) لدى المرضى في المجموعة G1 مقارنة بمجموعة السيطرة . في حين ارتفع مستوى انترلوكين 6 في مصل دم المجموعتين G1،G2 للذكور والاناث بالمقارنة مع مجاميع السيطرة . انخفض مستوى الببتيد الاذيني المدر للصوديوم في مصل دم المجموعةG1 مقارنة مع مجموعة السيطرة . في حين انخفض مستوى الصوديوم وارتفع مستوى البوتاسيوم في مصل دم المرضى مقارنة بمجموعة السيطرة .

Introduction

Atherosclerosis is a chronic inflammatory disease that affects the walls of the arteries, and is the underlying cause of cardiovascular disease [1]. Atherosclerosis occurs as a result of high levels of cholesterol in the blood, especially in people who have a high level of low density lipoprotein cholesterol (LDL-C), which is one of the risk factors for this disease [2] , A wide range of factors have been associated with the occurrence of atherosclerosis, these factors do not include only traditional risk factors such as hyperlipidemia, obesity, diabetes mellitus, high blood pressure, aging and smoking, but also include non-traditional risk factors such as infection and chronic inflammatory diseases [3].

High blood pressure is the basis for the emergence and development of atherosclerosis, as the heartbeat impulsive from the heart under high pressure leaves its impact with the passage of time on the walls of the arteries, which helps the accumulation of fatty deposits and cholesterol [4]. and that patients with high blood pressure show a rise in the concentration of cholesterol, and this rise is one of the main factors for increasing the risk of coronary heart disease and atherosclerosis [5].

Interleukin (IL-6) is a multidirectional cytokine that was originally identified in 1985 [6]. IL-6, cloned in 1986, is a glycoprotein peptide with a molecular weight of 26KD [7]. IL-6 exhibits both pro-inflammatory properties depending on the type of injury and the organ and cell in which it acts [8]. IL-6 is a major inducer of acute-phase protein synthesis by stimulating cells that can lead to fever and anemia [9]. IL-6 may have direct pro- and anti-atherosclerotic effects on processes associated with the development of atherosclerosis. The atherogenic effects include stimulation of vascular smooth muscle proliferation [10], and platelet activation [11], while anti-atherosclerotic effects include lowering of plasma low-density lipoprotein [12].

Material and Methods

Study Samples: The study was conducted on (60) blood samples were collected form private Hospital in the City of Tikrit and private laboratories , samples were divided into two groups: The first group (G1) which included 60 samples from Patients with atherosclerosis associated with hypertension and 30 samples of healthy people as a

control group (C).

Collection of blood samples and preparation:

Were taken serum (5) ml of the drawn blood and put it in a plastic tube with a tight-fitting lid and free of anticoagulant (Plain tube) left at room temperature until the blood coagulates and then put in a centrifuge at a speed of (4000) rpm for (15) minutes The blood serum was kept at a temperature of (-20) C until use and biochemical analyses. The blood samples were transferred in a cool box to the laboratory for testing.

Determination of Atrial natriuretic peptide, Interlukin-6 in serum

The concentration of each of (ANP , IL-6) was estimated according to the kit prepared from the Chinese company SUNLONG and using the ELISA technique using the double ELISA sandwich method for antibodies.

Determination of Electrolytes level in serum

The sodium level was estimated according to the kit equipped by the Egyptian company Vitro SCINT and according to the researcher›s method [13], and the potassium and chlorine levels were estimated according to the kit equipped by the Swiss company Agapp and according to the researcher›s method [14]15] ,].

Statistical analysis

The SPSS statistical program was used to find the mean± S.D as the special differences between the Two group were determined by using T. Test to show the difference between all groups at (P £ 0.05).

Results and discussion:

Estimation of Biochemical variables for the samples under study:

Table (1): the mean ± S.D of the IL-6 and ANP variables of the samples under study

Groups / Parameters	Mean ± SD		
	Control	**Patients**	**p-Value**
IL-6 (ng/L)	39.13±5.4	58.697.9±	**0.05**
ANP (Pg/ml)	36.88±4.72	26.41±3.31	**0.05**
Male			
IL-6(ng/L)	41.17±2.6	64.29±2.1	**0.05**
ANP (Pg/ml)	35.014±3.6	25.92±4.8	0.05
Female			
IL-6(ng/L)	38.73±2.4	57.63±3.1	**0.05**
ANP (Pg/ml)	35.19±3.1	26.11±3.8	**0.05**

P≥0.05

The results of the current research showed a significant decrease (P≤0.05) in Atrial natriuretic peptide level(26.41±3.31), and a significant elevated in IL-6 at p ≤ 0.05 (58.69±7.9) in patients with Atherosclerosis associated with Hypertension simile to healthy people (36.88±4.72), (39.13±5.4) . As Figures (1, 2) .

Also in the terms of gender , the result showed in table (1) a significant decrease (P≤0.05) ANP (25.92±4.8), (26.11±3.8) level and increase in IL-6 (64.29±2.1),(57.63±3.1) in the serum of males and females compared to healthy people (35.014±3.6), (35.19±3.1), (41.17±2.6), (38.73±2.4) ,with no significant differences between males and females.

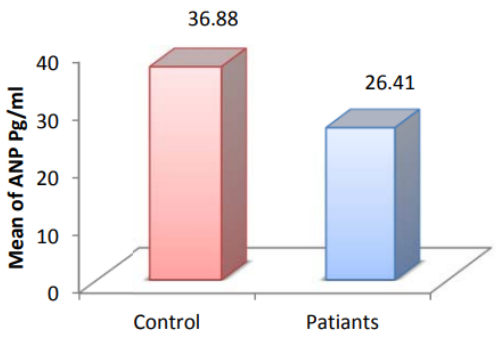

Figure 2: ANP in the blood serum for all group

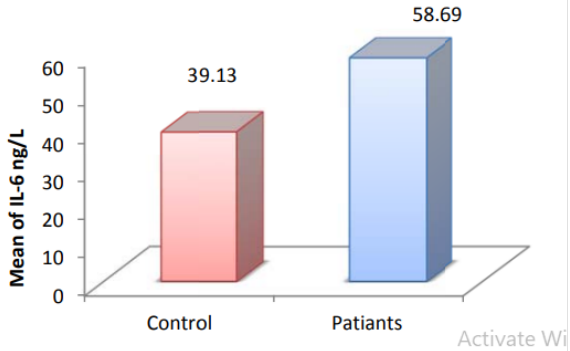

Figure 1: IL-6 in the blood serum for all groups

Also in the terms of Age , the result showed according to the table (2) a significant reduce in ANP in the serum of age group mentioned in the study compared to healthy subject , also the result showed a significant elevated in IL-6 in the serum of age group mentioned in the study compared to healthy subject.

Table (2): the mean - Standard deviation of IL-6 and ANP of the samples under study according Age

Parameter	Age	N	Control	N	Patients	P≥Value
IL-6 (ng/L)	40-55	13	38.04±1.7	22	57.11±2.0	0.05
	56-70	10	37.16±1.1	20	57.34±3.4	
	71-83	7	40.21±2.1	18	60.21±1.9	
ANP (Pg/ml)	40-55	13	36.90±4.83	22	26.22±2.76	0.05
	56-70	10	4.2536.82±	20	24.58±3.3	
	71-83	7	3.9135.68±	18	23.83±3.6	

Estimation of Electrolytes level for the samples under study:

Table (3) the mean ± S.D of the Electrolytes of the samples under study

Groups / Parameters	Mean ± SD		
	Control	**Patients**	**p-Value**
Na (mEq/l)	145.10±4.37	123.25±5.22	**0.05**
K (mmol/l)	4.310±0.510	8.53±2.142	**0.05**
Cl(meq/L)	102.33±4.19	113.46±3.11	**0.05**
Male			
Na (mEq/l)	148.05±3.42	121.11±2.01	**0.05**
K (mmol/l)	4.146±0.593	9.356±0.234	0.05
Cl (meq/L)	101.22±3.40	105.39±2.31	0.05
Female			
Na (mEq/l)	147.71±3.24	118.89±4.65	**0.05**
K (mmol/l)	4.332±0.331	8.147±0.724	**0.05**
Cl(meq/L)	102.80±2.73	114.80±3.76	**0.05**

The results of the current research showed a significant decrease at $p \leq 0.05$ in sodium level (123.25±5.22) and a significant elevated in potassium , chloride level (8.53±2.142), (113.46±3.11) in the serum of patients compered control subject (145.10±4.37), (4.310±0.510), (102.33±4.19). as figure (3, 4,5) .

Also in the terms of gender , the result showed in table (3) a significant decrease in sodium level (121.11±2.01), (118.89±4.65) and rise in Potassium, Chloride(9.356±0.234),(8.147±0.724), (105.39±2.31), (114.80±3.76) in the serum of males and females compared to healthy people.

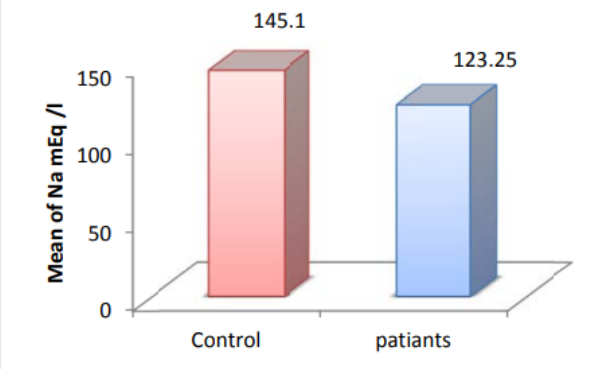

Figure 3: Na in the blood serum for all group

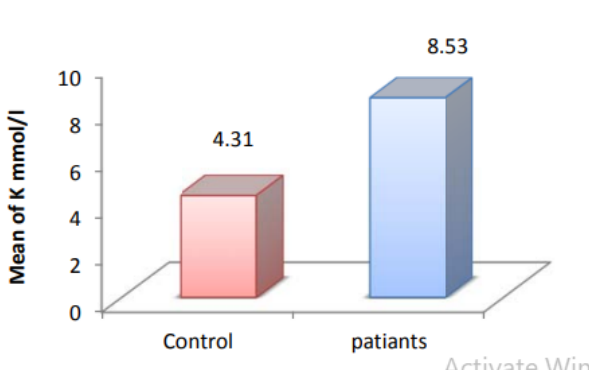

Figure 4: K in the blood serum for all group

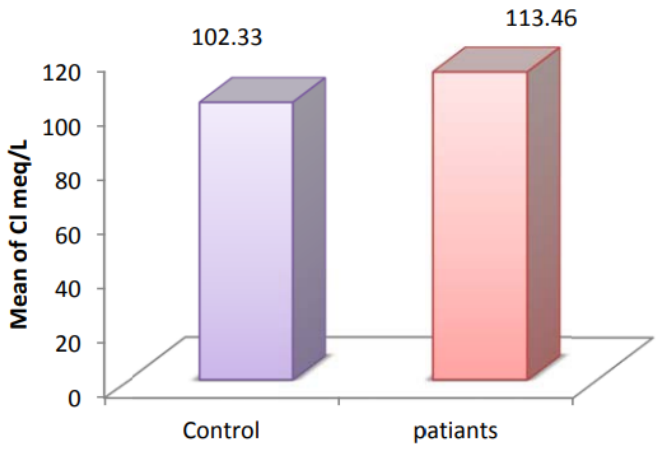

Figure 5:Chloride concentration in the blood for all group

Also in the terms of Age , the result showed according to the table (4) a significant decrease in sodium level and elevated in K, Cl in the serum of age group mentioned in the study compared to healthy people

Table (4): the mean ± S.D of Electrolytes of the samples under study according Age

Parameter	Age	N	Control	N	Patients	P≥Value
Na (mEq/l)	40-55 56-70 71-83	13 10 7	3.25146.11 ± 145.92±2.86 145.53±3.41	22 20 18	123.11±4.41 121.76±5.27 119.83±3.57	0.05
K (mmol/l)	40-55 56-70 71-83	13 10 7	4.231±0.224 4.325±0.310 4.756±0.478	22 20 18	8.465±0.724 9.025±0.211 9.240±0.523	0.05
Cl (meq/L)	40-55 56-70 71-83	13 10 7	99.024±2.05 101.21±1.94 102.11±2.17	22 20 18	112.67±2.14 112.92±3.05 113.69±3.43	0.05

Discussion

The results agreed with Al-Jumaili [16], who indicated that there was a decrease in the level of atrial natriuretic peptide in patients with heart failure. It was found in a study that patients with high blood pressure did not show any increase in ANP levels which may ex-

ert a compensatory response to their cardiovascular condition. They found that ANP deficiency may be associated with high blood pressure and increase the risk of cardiovascular disease. In addition, epidemiological studies revealed an inverse relationship between aldosterone levels and ANP in hypertensive subjects, with aldosterone as compared to atrial natriuretic peptide [17-18]. In addition, Gamaleldin [19] indicated that the gene expression of atrial natriuretic peptide was decreased in patients with high blood pressure. Natriuretic peptides are linked to several cardiovascular diseases including hypertension, atherosclerosis, heart failure, and stroke [20].

Fincheira [21] Gager [22] indicated that there was an increase in interleukin-6 level in patients with myocardial infarction. also indicated in his study that interleukin-6 levels play important roles in the risk of cardiovascular mortality in patients with chronic kidney disease.

Atherosclerosis is an inflammatory disease characterized by a chronic inflammatory process caused by several proinflammatory mediators, including cytokines [23]. Interleukin-6 is a coordinator of the inflammatory response and plays a major role in human atherosclerosis [24]. Therefore, IL-6 plays an essential role in atherosclerosis by causing endothelial dysfunction and enhancing the expression of adhesion molecules and the proliferation of smooth muscle cells [25-26], as studies have shown that interleukin-6 can promote the development and rupture of atherosclerotic plaques and thus accelerate the progression of atherosclerotic plaque growth and instability [27], so the results supported the increase in interleukin-6 in the blood risk of cardiovascular disease [28]. Feng *et al* [29] also indicated that elevated levels of interleukin-6 were associated with the occurrence of harmful remodeling of the left ventricle 6 months after myocardial infarction. Whereas, Topolyanskaya *et al* [30] indicated that high concentrations of interleukin-6 led to a 4.4-fold higher relative risk in patients with heart failure. It was also found that the activation of interleukin-6 signaling pathways is important in the process of atherosclerosis, plaque formation and instability, and inflammation in the arterial wall has been associated with cardiovascular disease [31]. Therefore, cytokinesis is associated with hypertension, heart fibrosis, atherosclerosis,

and cardiomyopathy [32].

The results do not agree with Al-Hamdany [33], who indicated the high level of sodium in patients with atherosclerosis. While the results were inconsistent with Wuopio [34] indicated in his study, which indicated that salt intake was associated with the risk of developing pressure and heart diseases. The association between salt intake and the risk of developing cardiovascular diseases was also explained, as it was found that high salt intake leads to an increased risk of coronary artery disease and atherosclerosis [34], and Peng [35] indicated the estimation of sodium intake on the basis of measured urine excretion, as the estimated high excretion levels of urinary sodium are associated with an increase in the presence of atherosclerosis. Therefore, the sodium intake estimated at 3-6 g per day leads to a lower risk of death and cardiovascular events compared to a level higher or lower than the intake [36] in the form of R, while I agreed with [37-38] who indicated in their study a decrease in the level of sodium as a result of reducing the intake of table salt for patients with high blood pressure. To lower sodium level in food intake and food intake in hypertensive patients. The reason for the low sodium level may be attributed to sodium depletion, especially in the case of acidosis, and this is due to impairment in tubular reabsorption of sodium [39].

Low sodium causes hypotension and stress reduction, which increases the permeability of the muscle cell (sarcolemma) of sodium [40]. Henley. As a result this leads to polyuria, hypothyroidism, hypokalemia, hypoglycaemia, and dehydration [41].

Researcher Wilcox also noted that sodium remains within normal limits in patients with high blood pressure, and attributed this to the use of diuretics, which, by weakening them to dilute the tubular fluid, will reduce the ability of the kidneys to quickly and effectively remove free water, and thus a slight and asymptomatic decline in sodium concentration will occur [42]. The reason for the decrease in the level of sodium in the current study may be that there is a close relationship between high blood pressure and dietary sodium intake for patients, as low dietary sodium not only reduces blood pressure and the incidence of high blood pressure, but is also associated with lower rates of morbidity and mortality from cardiovascular diseas-

es. A modest, prolonged reduction in salt intake leads to a related decrease in blood pressure in both hypertensive individuals, regardless of gender and ethnic group [43].

The results do not agree with Al-Hamdany [33], who indicated the low level of potassium in patients with atherosclerosis. These results are consistent with what was found by [44-45], who reported that patients with heart disease had lower levels of potassium. The reason behind this is that the renin-angiotensin system releases more of the hormone aldosterone, which leads to an increase in potassium excretion and estimation. The concentration of potassium in the blood serum decreases due to an increase in the permeability of potassium ions (K) with urine. In turn, it increases sodium ion retention, which leads to high blood pressure [46].

The results also agreed with Lu Xi [47] and Byrne [48], who indicated that the level of potassium is associated with high blood pressure, in addition to that, an imbalance in the level of the hormone aldosterone leads to an increase in the level of potassium [49-50]. Likewise, reducing the level of sodium that occurs by using diuretics or by reducing the intake of table salt (70-100 mmol) per day will reduce potassium excretion in the urine and prevent hypokalemia, and this is what he noticed [51].

The results do not agree with what was indicated by Humesh [50], which indicated an increase in the level of chloride in the blood serum of patients with myocardial infarction. The reason for the decrease in the concentration of chloride in the blood serum, may be attributed to the result of the decrease in the concentration of Apelin and the opposite occurs in the case of the increase in the concentration of Apelin according to the correlation equation. Chloride elevations occur in patients with heart disease as a result of the use of drugs that reduce blood volume and affect the concentration of ions in the blood serum and hypoxia and ischemia, which affects the permeability of ion membranes in muscle cells. For this reason [52], myocardial perfusion can restore the required balance of these ions in body fluids through the use of Apelin. Hypoxia regulates Apelin gene expression and secretion to myocardial cells [53].

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