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The Role of Atrial Natriuretic Peptide T Left Ventricular Function and Electrolyte Homeostasis in Congestive Heart Failure Patients

KEYWORDS: Congestive heart failure , ANP , Left ventricular ejection fraction

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ABSTRACT *Atrial natriuretic peptides(ANP) attract great attention in the last years. This interest is due to the fact that natriuretic peptides plays an important role on body fluids and electrolytes balance and on blood pressure homeostasis under normal physiological conditions as well as in a variety of cardiovascular diseases (CVDs),especially congestive heart failure.*

The present study was conducted on 100 subjects(50) patients with congestive heart failure (CHF) who admitted to the Coronary Care Unit, Medical wards and Echocardiography Unit at Ibn-Sena teaching hospital, Mosul, Iraq, from 1st October 2003 to 30th September 2004,and also (50) apparently healthy volunteers as control group included in this study.

The biochemical parameters were measured in plasma which include the concentrations of sodium (PNa), potassium (PK), creatinine (PCr), urea (PUr), osmolality (POsm), and ANP. The concentration of other parameters were also measured in urine including sodium (UNa), potassium (UK), osmolality (UOsm) and creatinine (UCr). Using plasma and urine values, calculation of creatinine clearance (CCr) and fractional excretion of sodium (FENa) were done. Echocardiographic assessment of left ventricular ejection fraction (LVEF) was also done.

In conclusion, plasma level of ANP was significantly elevated in patients with CHF and it could be considered as an important diagnostic and prognostic indicators especially in patients with CHF. A considerable degree of disturbance in body fluids and electrolytes balance together with significant reduction in renal function also occur in patients with CHF. The study further accentuates the essential role of ANP in the defense mechanisms against body fluids and electrolytes disorders in different CVDs including congestive heart failure patients.

Introduction and Review of Literature:
The normal heart secrete atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), the predominant members of a family of at least three structurally and functionally related hormones, they counteract cardiac over load by exerting a wide variety of effects on body fluids natriuresis, other electrolytes homeostasis and cardiovascular function[1,2].

Both hormones (ANP) and (BNP) have diuretic, natriuretic and antihypertensive effects by inhibiting the renine-angiotensin-aldosterone system (RAAS), they have renal sympathetic activity [3]. The hypotensive effect of these peptides is mediated primarily by a decrease in cardiac output brought by a reduction in intravascular volume [4].

Atrial natriuretic peptide is a potent vasodilator contributes in homeostatic regulation of body water, sodium , potassium and fat to lower blood pressure [4,5]. The concept of congestive heart failure (CHF) comprises both the primary distortion of blood flow and pressure which characterized cardiac impairment and secondary disturbance of electrolytes and water metabolism with subsequent activation of neuro-humoral systems[6]. Hyponatremia in (CHF) patients is usually hypoosmolal and it cause retention of water , the patient becomes edematous [7], which is further enhanced by a diuretic therapy especially in patients with impaired renal function[7,8]. Other studies considered hyponatremia as poor prognostic marker in patients with (CHF)[9].

Hyponatremia and hypokalemia are the most frequent electrolytes disorders encountered in (CHF)[10]. The kidney is the main organ involved during the course of (CHF), the decrease in renal blood flow will lead to decrease glomerular filtration rate (GFR), increase in tubular reabsorption of sodium and water with subsequent reduction of urine volume and urinary sodium excretion [11]. The difference in (GFR) in patients with (CHF) with different cardiac index of (1.5.2,and less than 1.5ml/min/1.73m^2) was reflected by the concentration of plasma urea (P_{Ur}) and plasma creatinine (P_{Cr})[12] .

Congestive heart failure is a neuroendocrine disorder both in relation to diagnosis and prognosis, it is found in experimental heart failure rats that (ANP) levels was 6.4 folds higher than that in normal rats. A marked increase of (ANP) plasma level was found in (CHF) patients by others with a positive correlation between (ANP) level and increased left and right atrial pressure [13] .

The left ventricular ejection fraction (LVEF) is the most widely used index of cardiac function which is important diagnostic, therapeutic and prognostic indicator of (CHF)[14]. Low ejection fraction was inversely correlated with marked increase in (ANP) in patients with (CHF), and was negatively associated with increased risk of hospitalization and death[15].

This study was conducted in attempt to evaluate the role of plasma (ANP) level in maintaining body fluids and electrolyte balance in the face of various pathophysiological mechanisms encountered during the course of (CHF), and to study the correlation of this novel (ANP) hormone as a possible biochemical indicator of the cardiac dysfunction with other indices of the left ventricular function like (LVEF%).

Subjects Materials and Methods :
After recording the routine information , concerning name ,age ,address , body weight , height and consent for every participant in the study a careful history and physical examination was performed ,they were asked about any past history of diabetes mellitus , ischemic heart disease and onset of the present illness. A general physical examination with special emphasis on reporting pulse rate , arterial blood pressure and the finding of heart auscultation.

This study was conducted on (100) subjects (50) patients with congestive heart failure (CHF) ,their age range between (25-70) years, their body weight was (52-100) kg , and height

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was(152-180) cm. The classification system that is most commonly used to quantify the degree of functional limitation imposed by heart failure based on the criteria of the New York Heart Association (NHA)[16] .This system assigns patients to one of four functional classes depending on the degree of effort needed to elicit symptoms :

Class 1: Symptoms of heart failure only at levels that would limit normal individual activities .

Class II: Symptoms of heart failure with ordinary exertion .

Class III: Symptoms of heart failure on less than ordinary exertion.

Class IV: Symptoms of heart failure at rest .

Depending on this classification the patients were divided in to four groups:

Group A Class I: This group included (22) patients with (CHF) aged (32-75) year (55.18±10.89), their body weight was(60-100)kg (74.90±10.48) and heights (152-180) cm. (166.90 ± 7.81).

Group B class II: This group included (11) patients with (CHF) aged (25-79) years (55.27±12.86) with body weight of (52-93) kg (68.54±13.7) and heights (155-180) cm. (167.45±9.00) .

Group C class III: This group included (8) patients with (CHF) aged (55-70)year (64.25 ±4.97) with body weights of (65-95) kg (73.25 ± 10.26) and heights (154-180) cm. (168±9.0) .

Group D class IV: This group included (9) patients with (CHF) aged (54-80)year (66,0 ± 8.58) with body weight (58-85) kg (68.88±8.65) and height (155-180)cm. (166.22±8.24).

The control group included (50) apparently healthy volunteers aged (24-67) year (45.76± 9.77) their body weights (54-92)kg (71.34±10.53) and heights (145-186) cm. (167.6± 9.73). All control subjects were scrutinized for the absence of any cardiac disease by thorough history and physical examination .

Chemical analysis:
1-Blood samples:10 ml. of blood was collected from every participant from anticubital vein. The blood samples were placed in 2 separate tubes containing lithium heparin. The tube used for estimation of the plasma (ANP) was placed immediately in the ice, the plasma was separated within 30 minutes by centrifugation at 3000 rpm for 10 minutes; the plasma samples were kept in capped plastic tubes in the deep freeze (-20 c°) until analysis.

The following plasma parameters were determined :

A- Concentration of sodium (mmol/L) (P_{Na})
B- Concentration of potassium(mmol/L) (P_K)
C- Concentration of creatinine (mmol/L) (P_{Cr})
D- Concentration of urea (mmol/L) (P_{Ur})
E- Osmolality (mosm /Kg) (P_{Osm})
F- Atrial natriuretic peptide (Pg /ml) (ANP)

2- Urine samples : Ten ml. of random urine samples were collected from patients and control groups .The urine samples were placed in capped plastic tubes and kept in deep freeze (-20C°) until analysis .

The following urinary parameters were determined :

A-Concentration of sodium in the urine (mmol/L) (U_{Na})
B- Concentration of potassium in the urine (mmol /L) (U_K)
C- Concentration of creatinine in the urine (mmol/L) (U_{Cr})
D- Urine osmolality (mosm/L) (U_{Osm})

Utilizing the urinary and plasma parameters together with age , body weight and height the following parameters were estimated :

a- Calculated creatinine clearance (C_{Cr} ml /min/1.73m2). A simple formula has been used that allows the (C_{Cr}) to be predicted by estimation from (P_{Cr}) [16].

C_{Cr}(ml/min) = 140-age(years) x lean body weight(Kg)/P_{cr}(mg/dl)x72

b- Fractional excretion of the filtered sodium (FE_{Na}%) ,it measures the percent of filtered sodium in the urine by the following equation [17].

$$FE_{(Na)}\ (\%) = (U_{Na} \times P_{Cr} / P_{Na} \times U_{Cr}) \times 100$$

Sodium and potassium concentrations were measured using an emission flame photometer (Corning 400,England). Plasma and urine creatinine were measured by Jaffe end point method using a kit from Biosyr following Kit procedure.

Plasma urea concentration was determined using a kit from Biocon (Germany). Plasma and urine osmolality were measured by freezing point depression technique using slamed osmometer (Bibbysterilin, France) .

Plasma aterial natriuretic peptide (ANP) level was determined by Enzyme Linked Immunosorbent Assay (ELIZA) utilizing kits provided by DRG international Inc. USA .

Left Ventricular Ejection Fraction (LVEF) was determined by echocardiography: Tow dimension and M-mode echocardiogram was obtained for every subject participate in the study , ejection fraction was derived from two dimensional apical tow and four chamber views for volume measurement.

Statistical analysis:
1. Post hog test was used to identify the differences in the mean of different parameters
2. Studentt-test (unpaired) was used.
3. Pearson correlation was performed to study the relationship between various parameters within each group .
4. All values were expressed as mean ± SD.

Results:
The mean ± SD of all studied parameters in patients with congestive heart failure (CHF) and the control group, and the level of significance between the two groups was shown in table (1):

There is a highly significant differences ($P \leq 0.00$) between CHF and the control in the plasma concentration of sodium (P_{Na}) , osmolality (P_{Osm}), creatinine (P_{Cr}) , urea (P_{Ur}) , atrial natriuretic peptide

Level (ANP) and left ventricular ejection fraction (LVEF %) . Also the urine concentration of sodium (P_{Na}),

(U_{Osm}) , (C_{Cr}) , and fraction excretion of sodium (FE_{Na}%) show a highly significant differences ($P \leq 0.001$) between the two studied groups , The plasma concentration of potassium (P_K) was significantly different between the two groups at ($P \leq 0.05$), No significant differences was seen in the concentration on urine potassium (U_K) and creatinine (U_{Cr}) between both groups .

Table (1) : Comparison of different parameters between (CHF) group and control group.

Parameters	Mean ± S.D.		P value
	Group I (CHF) N=50	Control group N=50	
P_{Na}mmol/L	138.46 ± 3.48	140.67 ± 1.21	P<0.0001

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$P_K$mmol/L	3.94 ± 0.62	4.16 ± 0.30	P<0.05
P_{Osm}mosm/kg	281.00 ± 9.16	288.12 ± 6.30	P<0.001
P_{Cr} µmol/L	80.64 ± 8.87	70.66 ± 6.85	P<0.0001
P_{Ur}mmol/L	4.57 ± 0.68	3.43 ± 0.56	P<0.0001
U_{Na}mmol/L	108.91 ± 16.19	136.03 ± 26.08	P<0.0001
$U_K$mmol/L	59.64 ± 16.67	72.26 ± 15.98	NS
U_{Osm}mosm/kg	607.00 ± 110.39	741.80 ± 91.88	P<0.0001
U_{Cr}mmol/L	7.90 ± 1.22	7.83 ± 1.67	NS
C_{Cr} ml/ min/1.73m^2	89.14 ± 9.23	111.03 ± 13.70	P<0.0001
FE_{Na}%	0.80 ± 0.085	0.87 ± 0.064	P<0.0001
ANP pg/ ml	97.40 ± 30.81	37.54 ± 7.18	P<0.0001
LVEF%	37.1 ± 7.34	64.65 ± 4.09	P<0.0001

Table (2) **:**Show the correlation between different parameters within Patients group **:**

- **i.** There were significant positive correlations between P_{Osm} and both P_{Na} and P_K (r = 0.75, p<0.0001 and r = 0.41, p < 0.005) respectively.
- **ii.** There was significant positive correlation between P_{Na} and P_K (r= 0.41, p <0.005).
- **iii.** There were significant negative correlations between P_{Cr} and both U_{Na} and U_K (r = -0.44, p<0.001and r = -0.29, p< 0.05). There was also a significant negative correlation between P_{Cr} and U_{Osm} (r = -0.29, p< 0.05).
- **iv.** There were significant positive correlations between U_{Na} and both U_{Osm} and FE_{Na} (r = 0.37, p<0.01 and r = 0.39, p < 0.005) respectively.
- **v.** There was significant positive correlation between C_{Cr} and both P_K and U_{Osm} (r = 0.34, p<0.01 and r = 0.39, p< 0.005) respectively.
- **vi.** There was significant negative correlation between C_{Cr} and P_{Cr} (r = -0.28 , p < 0.05), and a significant positive correlation between C_{Cr} and FE_{Na} (r = 0.38 ,p< 0.01).
- **vii.** There was significant negative correlation between plasma ANP level and LVEF (r = -0.83, p<0.0001), and between ANP and C_{Cr} (r = - 0.37, p< 0.01).

	P_K mmol/l	P_{Osm} mosm /kg	P_{Cr} µmol/l	C_{Cr} ml/min/1.73m^2	U_{Osm} mosm/kg	U_{Na} mmol/l	FE_{Na} %	LVEF %
ANP pg/ml	NS	NS	NS	-0.37**	NS	NS	NS	-0.83**
P_{Na} mmol/l	0.41**	0.75**	NS	NS	NS	NS	NS	NS
P_K mmol/l		0.41**	NS	0.34*	NS	NS	NS	NS
P_{Cr} µ mol/l	NS	NS		-0.28*	-0.29*	-0.44**	NS	NS
C_{Cr} ml/ min/1.73m^2	0.34*	NS	-0.28*		0.39**	NS	0.38**	NS
U_{Osm} mosm/kg	NS	NS	-0.29*	0.39**		0.37**	NS	NS
U_{Na}mmol/l %	NS	NS	-0.44**	NS	0.37**		0.39**	NS
U_k mmol/l	NS	NS	-0.29*	NS	NS		NS	NS
FE_{Na}	NS	NS	NS	0.38**	NS	0.39**		NS

Table (2): Correlation coefficient between different parameters within patients
NS : non-significant correlation.

*** Correlation is significant at the P< 0.05 level.**
**** Correlation is significant at the P< 0.01 level.**

Comparison between groups A , B, C and D (CHF) patients:
The detailed results of these groups are given in table (3). The differences between group A, B, C and D were studied using ANOVA test (one way analysis of variance) and further analyzed by LSD test, the results showed the following differences**:**

- **i.** There were significant differences in P_{Na} between the four subgroups (F= 10.05, p< 0.001). P_{Na} was significantly higher in group II A than that in group C and D (p< 0.001 and p< 0.0001) respectively. It was also significantly higher in group B than in group D (p < 0.05).
- **ii.** There were significant differences in P_{Osm} between the four subgroups (F = 9.20, p< 0.0001). P_{Osm} was significantly higher in group A than that in group C and D (p < 0.005 and p <0.001) respectively.
- **iii.** There were significant differences in P_{Cr} between the four subgroups (F=18.5, p<0.0001). P_{Cr} was significantly lower in group A than that in group B, C and D (p < 0.0001). It was also significantly lower in group B than that in group D (p<0.05).
- **iv.** There were significant differences in P_{Ur} between the four subgroups (F = 14.1, p < 0.0001). It was significantly lower in group A than that in group B, C and D (p< 0.005, p<0.0001 and p< 0.0001) respectively.
- **v.** There were significant differences in U_{Na} between the four subgroups (F=23.6, p< 0.0001). U_{Na} was significantly lower in group A than that in group B, C and D (p< 0.005, p < 0.0001 and p <0.0001) respectively. It was also significantly higher in group B than that in group C and D (p < 0.01and p < 0.0001) respectively.
- **vi**. There were significant differences in U_K between the four subgroups (F = 5.5, p < 0.002). U_K was significantly higher in group A than that in group C and D (p< 0.05).
- **vii.** There were significant differences in U_{Osm} between the four subgroups (F =11.6, p<0.0001). U_{Osm} was significantly higher in group A than that in group B, C and D (p < 0.001)
- **viii.** There were significant differences in C_{Cr} between the four subgroup (F = 22.8, p < 0.0001). C_{Cr} was significantly higher in group A than that in group B, C and D (p < 0.0001). It was also significantly higher in group B than in group D (p<0.001) and in group C than in group D (p< 0.01).
- **ix.** There were significant differences in FE_{Na} between the four subgroups (F= 19.0, p<0.0001). FE_{Na} was significantly higher in group A than that in group B, C and D (p<0.001).
- **x.** There were significant differences in ANP between the four subgroups (F=22.4, p <0.0001). Plasma ANP was significantly lower in group A than that in group B, C and D (p<0.05, p<0.0001) respectively. It was also significantly lower in group B than in group C and D (p< 0.0001) .
- **xi.** There were significant differences in LVEF between the four subgroups (F= 27.5, p<0.0001). LVEF was significantly higher in group A than that in group B, C and D (p<0.0001). It was also significantly higher in group B than in group C and group D (p<0.05).

Table (3): Comparison of different parameters between group A, group B, group C and group D.

Parameters	Mean ± SD			
	Group A CHF (Class I) N = 22	Group B CHF (Class II) N = 11	Group C CHF (Class III) N = 8	Group D CHF (Class IV) N = 9
PNa mmol/L	140.42 ±31.99[a]	139.00 ±2.82[c]	136.15 ±4.49	135.05 ±2.57
PK mmol/L	3.86 ± 0.54	4.01±0.57	3.90 ± 0.73	4.11 ± 0.82

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POs mmosm/kg	286.68 ±8.06[a]	279.90 ±7.56	274.25±7.88	274.00±4.60
P_{Cr} µmol/L	74.17 ± 6.53[b]	83.56 ±7.03[c]	84.15 ±4.63	89.76 ± 8.36
PUr mmol/L	4.25 ± 0.42[b]	4.56 ±0.22	4.87 ±0.19	4.98 ± 0.16
UNa mmol/L	121.73±11.85[b]	109.78±11.52[d]	95.11±9.90	88.77 ±7.41
UK mmol/L	68.73 ±16.38[a]	56.63 ±12.15	52.25±16.37	47.66 ±11.26
UOsm mosm/kg	684.13±99.46[b]	571.4 ±67.40	541.25±74.62	520.44±63.62
U_{Cr} mmol/L	7.85 ±1.06	7.88 ±1.11	7.81 ±1.35	8.13 ±1.32
C_{Cr} ml/min/1.73 m^2	96.60 ±7.86[b]	86.64 ±5.83[c]	85.52 ±4.13[e]	77.05 ±2.77
FE_{Na} %	0.87±0. 04[b]	0.78 ±0. 08	0.74 ±0.06	0.72 ± 0.05
ANP pg/ ml	76.04 ±15.24[b]	93.00 ±19.40[d]	131.14±23.05	125.00±26.65
LVEF %	43.09 ± 4.28[b]	35.90 ±3.96[d]	30.87 ±3.97	29.22 ±5.91

a : significantly differ in group A from respective values in group C & D.
b : significantly differ in group A from respective values in group B, C,D.
c : significantly differ in group B from respective values in group D .
d : significantly differ in group B from respective values in group C& D .
e: significantly differ in group C from respective values in group D.

The congestive heart failure patients(CHF)were divided into four groups (A, B, C, and D) according to the severity of the disease depending on (NHA) classification (class one to four)

Fig (1) : Show the mean plasma (ANP) concentration that was higher in group (D)it was(130 pg/ml) compared to other three groups, the lowest value of plasma (ANP) concentration was (72 Pg/ml) seen in group (A) and differ significantly from respective values in groups (B, C and D).Plasma concentration of (ANP) in group (B) differ significantly from groups (C and D) .

Fig (2) : Show the mean values of creatinine clearance (C_{Cr}) in the four groups values in group (A) was higher than its value in other three groups and differ significantly from group (B, C and D),while (C_{Cr}) in group (B) differ significantly from group (D) .Creatinine clearance in group (C) also differ significantly from its value in group (D), highest creatinine clearance which was (98/ml/min/1.73m^2) was detected in group (A) compared to its mean lowest value that was (76/ml/min/1.73m^2) seen in group(D).

Fig (3) : Show the mean values of left ventricular ejection fraction (LVEF%) in the four groups, its values in group (A) differ significantly from its respective values in groups (B, C and D) . Also significant difference in (LVEF%).

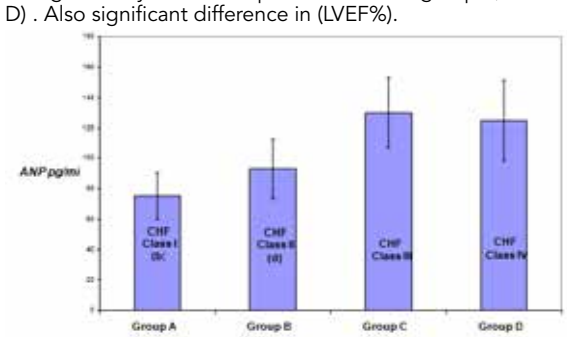

Fig.(1) : Mean values of atrial natriuretic peptide (ANP) in group A, B, C and D. (b: significantly differ in group A from respective values in group B, C and D, d: significantly differ in group B from respective values in group C and D).

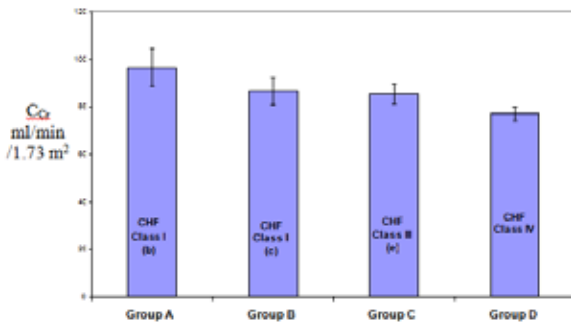

Fig.(2) : Mean values of creatinine clearance (Ccr) in group A, B, C and D.(b: significantly differ in group A from respective values in group B, C and D, c: significantly differ in group B from respective values in group D and e: significantly differ in group C from respective values in group D).

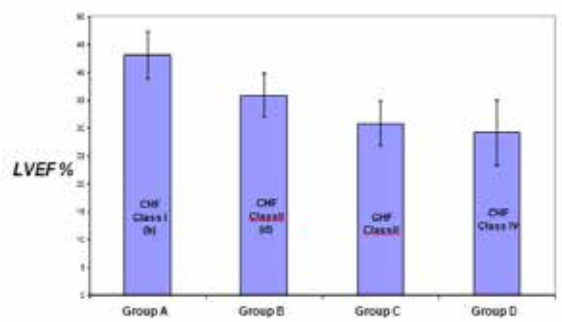

Fig.(3) : Mean values of left ventricular ejection fraction (LVEF%) in group A , B, C and D. (b: significantly differ in group A from respective values in group B, C and D, d : significantly differ in group B from respective values in group C and D).

Discussion:

A-Body fluids and electrolytes:

The mean plasma sodium (P_{Na}) , and urine sodium (U_{Na}) in congestive heart failure (CHF) was lower than the control group .twenty eight percentage (28%) of studied patients showed hyponatremia while the remaining patients have normal levels of plasma sodium. Hyponatremia is common in (CHF) patients; this result from an inability of the kidney to excrete ingested water which is largely related to the associated fall in cardiac output and systemic blood pressure that stimulate secretion of the hypovolemic hormone renine[18]. With a subsequent increase in angiotensin II formation, ADH and norepinephrine[18,19].

The neurohumoral changes that are induced limit both sodium and water excretion in an attempt to return perfusion pressure to normal [20] .

Potassium predominantly an intracellular cation, (23%) of patients with (CHF) had hypokalemia ; dyshypokalemia had a serious dysfunction of the cardiac muscle and cardiac rhythm disorder with considerable morbidity and mortality. Potassium imbalance in (CHF) patients is largely due to alteration in urinary potassium excretion, all of the filtered potassium is reabsorbed in the proximal tubule and loop of Henle.

Urinary potassium is determined by potassium secretion from the cells of distal renal tubule and to less extent collecting ducts [17].

The mean plasma level of atrial natriuretic peptide (ANP) in patients with (CHF) is significantly higher than the control (P≤0.0001),and as this hormone is a potent natriuretic pep-

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tide[5,20] accordingly one may postulate that patients with (CHF) should have the level of sodium in the urine (U_{Na}) higher than that of the control group , in spite of significantly high level of (ANP), the majority of (CHF) patients avidly retain sodium and water, therefore there is no renal response to (ANP) and this is proved by experimental animals that had extreme decline in renal response to high levels of (ANP)[21, 22].

Patients with (CHF) presented with low (U_{Na}) and fraction excretion of sodium % (FE_{Na}%) . the plasma osmolality value (P_{OSm}) in patients was significantly less than its value in the control group (P≤0.0001), (14%) of the patients have hypoosmolality, they were either hyponatremic or had (P_{Na}) lower than patients with normal (P_{OSm}) .

B- The plasma creatinine , urea and creatinine clearance :
The mean creatinine clearance (C_{Cr}) in patients with (CHF) was significantly lower than the control group and (C_{Cr}) was much lower in severe cases of (CHF) compared with mild cases , the degree impairment of renal function in (CHF) patients is directly related to the severity of the disease[23], and significant negative correlation between (ANP) and (C_{Cr}) was observed ,atrial natriuretic peptide play an important role in preserving the cardio-renal homeostasis of renal blood flow[24, 25]. recent studies showed that the physiological function of (ANP) is blunted in patients with (CHF) like decreased renal tissue sensitivity to the hormone and failure of the atrial myocytes to further enhance the rate of secretion of this hormone in advance cases of congestive heart failure[26,27].

The plasma level of urea was abnormally high in (16%) of the patients with (CHF),accordingly impaired (GFR) and tissue wasting observed during the course of the disease raises the possibility that increased urea production may be chiefly responsible[28] the raise in (P_{Ur}) level could be due to decrease (GFR) , increased urea production or a combination of both these factors.

C- Atrial Natriuretic Peptide (ANP) :
The mean plasma (ANP) in patients with (CHF) was significantly higher than that of the control and it was much higher in severe cases (group D) compared with milder cases (group A). Furthermore a significant negative correlation was found between plasma (ANP) and left ventricular ejection fraction in (CHF) patients , these results are consistent with the findings of other investigators[14,29]. It is found that cardiac and circulating (ANP) are significantly increased in heart failure and directly correlated with the severity of the disease[3 , 22,, 30] . Inspite of high concentration of (ANP) in these patients the retention of water and sodium are relentless and lead to worsening of heart failure; it is recorded an impairment in urinary excretion of sodium in response to infused (ANP) in patients with (CHF) compared to normal [31] .

trials of an endopeptidase inhibitor and Candoxatrilat in patients with (CHF) have shown an elevation of (ANP) levels associated with an increase in urine volume and urine sodium excretion together with clinical improvement[31,32] .

D- Left Ventricular Ejection Fraction (LVEF):
Echocardiography is of crucial importance in patients with (CHF) ,it is estimated at best that the clinical diagnosis is not so accurate in about (50%) of patients, accordingly an objective measurement of left ventricular function is essential for improving the accuracy of diagnosis[16]. The mean value of (LVEF) in congestive heart failure patients was significantly lower than the control, negative correlation between the plasma level of (ANP) and (LVEF) was seen in (CHF) patients , therefore measurement of plasma (ANP) may be of value in determining the severity of congestive heart failure especially when the facility for performing of echocardiography is not available .

In conclusion, plasma levels of (ANP) was significantly elevated in patients with (CHF); patients with severe (CHF) tend to exhibit a higher level of (ANP) than mild cases. A negative correlation between (ANP) and (LVEF) was seen in(CHF) patients ,thus higher plasma (ANP) could be regarded as an important diagnostic and prognostic indicator of cardiac dysfunction in these patients. A significant negative correlation between (ANP) and creatinine clearance was also noted , a disturbance in body fluids, electrolyte balance together with reduction in renal function accentuates the inverse relationship between (ANP) and renal function , (ANP) has essential role in the defense mechanism against body fluids and electrolytes disorders in congestive heart failure patients.

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