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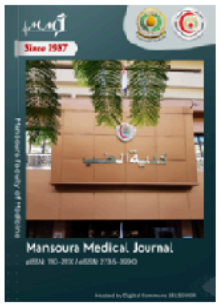

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ABSTRACT

Elevated levels of plasma atrial natriuretic factor (ANF) were found in cirrhotic patients. Some investigators reported basal levels, while other reported low levels of ANF.

This lead us to investigate the effect of bilaharzial periportal fibrosis (BPD) and bilharzial liver cirrhosis and posthepatitic cirrhosis on plasma ANF.

27 patients were selected and divided into three groups. The first group comprized nine patients of bilharzial periportal fibrosis. The second group comprized 9 patients of mixed cirrhosis without ascites. The third group comprized 9 patients of mixed cirrhosis and ascites.

ANF was measured by radioimmunoassay. Abdominal and cardiac ultrasonography was used for measurement of liver size and echogenicity together with diameter of portal vein, splenic view and cardiac chambers.

The results showed that ANF was reduced in all group of patient except those developing ascites, they showed levels slightly more than the control group.

INTRODUCTION AND AIM OF THE WORK

One of the most exciting recent major advance in physiology and

medicine was made when natriuretic granules were discovered in the atria of the heart (Mills, 1984).

Elevated levels of plasma atrial natriuretic factor (ANF) were found in cirrhotic patients (Fernandez-Grus et al., 1985), some investigators such as Burghardt et al., 1988a and Salerno et al., 1990) found basal plasma level sirtlialr to control subjects in cirrhotic patients without ascites. Only one group of workers showed slightly lower ANF in ascitic patients (BanKovsky et al., 1986).

The present work is a trial to study the possible changes in plsma ANF in patients with hepatosplenic bilharziasis with and without liver cirrhosis, with and without ascites, and the potential role of ANF in the pathogenesis of impaired sodium homeostasis in such patients.

Materials:

The present study comprised 27 patients of both sexes with age ranging from 16-55 years and 9 healthy subjects of matched age and sex as control group. The patients were divided into three groups :

Group I: 9 patients with pure bilharzial periportal fibrosis (BPF).

Group II: 9 patients with mixed BPF and post hepatitic cirrhosis without ascites.

Group III: 9 patients with mixed BPF. and post hepatitic cirrhosis with ascites.

All patients were subjected to thorough history taking and clinical examination. Patients with present and past history of cardiac and renal diseases were excluded as well as hypertensive patients and females on pills. Both patients and control were on normal sodium diet. Drug therapy, especially diuretics, were stopped at least one week before blood sampling.

The diagnosis of bilharzial aetiology is based upon history of bilharziasis and its treatment, urine and stool analysis for bilharzial ova, irnmunodi-

agnosis of schistosomiasis and liver biopsy. The diagnosis of post hepatitic cirrhosis is based upon the clinical history of hepatitis, elevated serum bilirubin and transominases, positive markers of B&C viruses and by liver biopsy.

Methods:

a) Analytic methods:

1- Plasma immunoreactive (PIR) atrial natriuretic factor using radioimmunoassay (RIA) kits provided by Peninsula laboratories Inc.

2- Serum creatinine estimation (Langley & Evans, 1963).

3- Serum and urinary sodium estimation using KNA radiometers.

4- Serum albumin by biodynamic unitest system (Doumas & Biggs, 1972).

5- Serum bilirubin by colorimetric method described by Ferro & Ham, (1963).

6- Serum transaminases by the method described by Ritman & Frankel, 1957.

7- Vinal markers.

8- Serological diaynosis for schistosoma mansoni.

b) Liver biopsy.

c) Abdominal ultrasonography for;

I) Size & Echogenicity of the liver and spleen.

2) Portal vein diameter (PVD).

3) Splenic vein diameter (SVD).

d) Echocardiography for;

I) Left atrial diameter (LAD) range 2.3 - 4.4 cm.

2) Right ventricualr dimension (RVD range 0.7 - 2.3cm. The measurements are according to Feigenbaum, 1986.

E) Statistical analysis using;

I) Unpaired T-Test.

2) One way analysis of variance using scheffe method.

RESULTS

Are tabulated in tables (1-4).

DISCUSSION

The low level of ANF found in our patients in groups I & II can be explained by insufficient stimulation for ANF release. In these two groups of patients there is significant decrease in serum albumin which leads to decreased circulating blood volume.

Another possible explanation for the reduced level of ANF is the increased capacity of the circulation. These patients suffer from huge portosystemic shunting and huge collateral circulation as evidenced by the significant increase in portal vein and splenic vein diameter, serving to sequesterate blood away from the heart.

The proposal that the decreased circulating blood volume and/or increased capacity of the circulation as a cause for reduced ANF level, is faced by another contradictory findiny, that is to say, the significant increase in left atrial diameter. According to Mebazaa and Payen, 1990, ANF must be increased rather than to be decreased, these workers suggested that atrial distension is the main stimulus for ANF rlease.

The increased left atrial diameter observed in this work is in agreement with that of Rector & Hossack, 1988 and Rector et al. l990. They found that patients with alcoholic liver cirrhosis have significant larger left atrial diameter in cases with and without ascites.

The dissociation between plasma ANF and left atrial diameter has been reported by several authors such as Au et al. l9gO; Berglund et al., 1990 and Nakamura et al., 1990. Only Matsubara et al., 1987 revealed that elevation of atrial (Principally left atrium) pressure stimulates ANF secretion in man.

With progression of cirrhosis and development of ascites ANF again begins to increase significantly in

patients of group III as regard non ascitic patients of group I and II. This is not astonishing because with progression of liver cirrhosis there is more reduction in serum albumin, accordingly there will be more decrease in circulating blood volume. The body senses the hypovolemia as stress which results in persistant stimulation of stressfull mechanisms such as sympathetic stimulation, activation of renin angiotensin aldosterone (RAA) system, ADH and cortisol.

These neurohumoral and hormonal factors are supposed by Ballerman et al. 1986 and Gardner et al., 1988 to have direct stimulatory effect at the level of myocytes to incraese ANF synthesis. Klemin et al. 1988 mentioned that angiotensin II (AII) increase ANF level especially when blood volume is low. Ballerman suggested that ANF acts as a counter mechanism against stress. It is released by the stressfull hormones themselves to check and pervent the overshooting of these stressfull substances.

Laragh et al., 1986 mentioned 4 different ways by which ANF counteracts or opposes RAA system -1- by reducing renin secretion -2- by relaxing angiotensisn contracted vessels -3- by blocking angitensin induced aldosterone synthesis and -4- by its natriuresis opposing aldosterone induced sodium retension. So in volume contracted disorders the neurohumoral and hormonal factors, not the atrial distension, can be the main stimuli for ANF release.

In cirrhotic patients of the group III, there is marked decrease in urinary sodium excretion inspite of the marked enhancement of ANF level which is supposed to act in the way of increasiny urinary sodium excretion. Schowalter et al., 1988 reported attenuated natriuresis to ANF in the presence of intra-renally infused angiotensin II, also MC Murray and Struthers, 1988 showed that the renal effects of ANF were reduced in the presence of simultaneously elevated level of angiotensin II.

These previous observations could explain the blunted natriuresis in cirrhotic ascitic patients inspite of the marked enhancement of ANF level, especially in patients having high renin angiotensin aldosterone activity.

Table (I) : Comparison between different groups of patients (Gp. I, II, III) and control group according to biochemical data.

Group		Variable			
		ANF	S. Na	Una	S. alb.
Control	Mean	232.4	136.7	151.6	4.3
	SD±	43.6	3.16	26.8	0.27
Gp. I	Mean	173.3	136.7	145.9	3.77
	SD±	25.6	5.94	28.8	0.56
	P	<0.001	0	>0.05	<0.05
GP. II	Mean	176.6	131.2	114.6	3.4
	SD±	25.7	3.8	26.7	0.35
	P	<0.001	>0.05	<0.001	<0.001
Gp. III	Mean	273.4	122.2	50.18	2.9
	SD±	87.6	4.17	15.9	0.27
	P	>0.05	<0.01	<0.001	<0.001

ANS = Atrial natriuretic factor pg/ml.
S. Na = Serum sodium concentration meg/L.
UNa = Urinary sodium excretion meq/day.
S. alb = Serum albumin gm/dl.

Table (2) : Comparison between group I, II, III of patients acccrding to biochemical data by biochemical data by one way analysis of variance.

Variable		Group GP I	GP II	GP III	P	
ANF	Mean	173.2	176.6	273.4	<0.001	I, III
	SD±	35.6	25.7	87.6		II, III
S> Na	Mean	136.7	131.2	122.2	<0.003	I, iII
	SD±	5.9	3.8	4.17		
U. Na	Mean	145.9	114.6	50.18	<0.001	I,II,III
	SD±	28.3	26.7	15.9		
S. alb	Mean	3.77	3.4	2.9	<0.008	I,III
	SD±	0.55	0.35	0.27		

I, III = The compairson made between groups I, IIII is significant.
II, III = The compairson made between groups II, IIII is significant.
I, II, III = The compairson made interbetween different grcups is significant.

Table (3) : Comparison between groups (I, II, III) of patients and control group according to abdominal U/S & Echocardiographic parameters.

Group		Variable			
		PVD	SVD	LAD	RVD
Control	Mean	0.94	0.74	3.12	1.8
	SD±	0.1	0.12	0.19	0.12
Gp. I	Mean	1.87	1.7	3.7	1.77
	SD±	0.87	0.33	0.41	0.16
	P	<0.001	<0.001	<0.01	>0.05
GP. II	Mean	1.96	1.83	3.71	1.88
	SD±	0.19	0.39	0.31	0.35
	P	<0.001	<0.001	<0.01	>0.05
Gp. III	Mean	1.63	1.26	3.17	1.82
	SD±	0.43	0.22	0.5	0.12
	P	<0.001	<0.001	>0.05	>0.05

PVD = Portal vein diameter in cm.
SVD = Splenic vein diameter in cm.
LAD = Left atrial diameter in cm.
RVD = Right ventricualr diamension in cm.
U/S = Ultrasonography.

Table (4) : Comparison between group I, II, III of patients according to abdominal U/S and Echocardiographic parameters by one way analysis of variance.

		Group				
Variable		GP I	GP II	GP III	P	
PVD	Mean	1.87	1.96	1.63	<0.1	
	SD±	0.27	0.19	0.43		
SVD	Mean	1.7	1.83	1.26	<0.002	I, III
	SD±	0.33	0.39	0.22		II,III
LAD	Mean	3.7	3.71	3.17	<0.01	I, III
	SD±	0.41	0.31	0.5		II,III
RVD	Mean	1.77	1.88	1.82	<0.06	
	SD±	0.16	0.35	0.12		

I, III = The compairson made between groups I, IIII is significant.
II, III = The compairson made between groups II, IIII is significant.

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