STUDIES ON LIVER FUNCTION TESTS IN ESSENTIAL HYPERTENSION.

By

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An interrelationship between the functional integrity of the liver and development and maintenance of hypertension is being increasingly recognised (Raaschou, 1954; Loyke, 1955). An absence of experimental and clinical hypertension with liver disease has been noted (Bouchnut, et al, 1937; Spatt, et al, 1949). It was suggested that hypertension could not occur in the presence of more than minimal liver damage (Raaschou, loc cit) and, conversely, a deranged liver would afford a good degree of protection against this syndrome (Loyke, loc cit). The current trends have recently been summarised (Brit. Med. Jour.,1956).

During the last few years we have been investigating cases of hepatic cirrhosis (Das Gupta, et al, 1953 ; Wig, et al, 1954). On review of the case histories, it was observed that none of the 62 cases investigated had blood pressure readings higher than 150/90 mm. of Hg. A majority of the patients (74.2%) were in the fourth decade or over.

In view of this it was decided in 1954 to work on converse lines, viz., to investigate hepatic functions in cases of established essential hypertension.

METHODS AND MATERIALS

31 cases of essential hypertension between the ages 25-60 years, were selected from the Cardiology Clinic of the V. J. Hospital, Amritsar. Cases with any evidence of renal disease or congestive heart failure were not included in this study. Adrenal-cortical function was also assessed in 25 of the cases (Das Gupta, et al, 1955).

All the cases were subjected to a battery of liver function tests, viz., serum bilirubin ; total and differential serum proteins with albumin : globulin ratio ; cephalin-cholesterol flocculation ; thymol turbidity and flocculation and urinanalysis for bile salts, pigments and urobilinogen carried out by the usual methods (Das Gupta, et al, 1953).

RESULTS

The distribution of the cases according to sex was 19 males and 12 females. The distribution according to age was :

20 – 29	years	..... 4 cases.
30 – 39	years	..... 4 ,,
40 – 49	years	.....12 ,,
50 – 60	years	.....11 ,,

The results of the various liver function tests performed on patients suffering from essential hypertension are presented in Table I and their comparative values in Table II. In Table III is presented the data of case No. 31 before and during hepatic phase.

DISCUSSION

In the current study it is evident from Table I that liver parenchyma was functioning normally in most of the cases of essential hypertension. However, the thymol turbidity and serum albumin : globulin showed a slight shift from the normal limits in some of the cases, including case No. 31 who later on developed severe hepatitis with a concomittant fall in blood presure. This would tend to support the hypothesis that a normally functioning liver, or a liver with a minimal damage, is essential both for the maintenance of normal blood pressure and development of hypertension. And conversely, an abnormal liver may have certain compensations, as is evident from case No. 31 in Table III. The history of case No. 31. is as below :

H. K., 43 years old female, suffering from essential hypertension, was under observation in the Cardiology Clinic for 1½ years. In January, 1956, she was admitted for treatment. Her blood pressure readings ranged between 210–250/120–136 mm. of Hg. She was treated with Reserpine, Hydergine and Methonium compounds, but the blood pressure did not show any significant drop. After about 2 months stay she was discharged from the hospital with her blood pressure level at 220/120 mm. of Hg. She continued to take a combination of Reserpine and Hydergine, but the blood pressure never dropped below 220/120 mm. of Hg.

On August 10, 1956, she developed fever with occasional vomiting and loss of appetite. Two days later jaundice was noticed and a few days after she was admitted into the hospital. At the time of admission she was fully conscious and had moderately deep jaundice. Liver was palpable, 3 fingers, firm and somewhat tender. Blood pressure recorded 150/95 mm. of Hg. During

Table I

No.	Case	Age Sex	T. serum bilirubin mg%	T. serum protein Gm%	Serum albumin Gm%	Serum globulin Gm%	Albumin: Globulin Ratio	Cephalin-Cholesterol Flocculation 24 hrs	Cephalin-Cholesterol Flocculation 48 hrs.	Thymol Turbidity and Flocculation Maclagan Units	Thymol Turbidity and Flocculation 18 hrs.	Urinanalysis
1	B. S.	45 M	0.2	6.8	3.6	3.2	1.1	—	±	5.0	—	Normal
2	G. S.	30 M	0.1	6.1	3.1	2.9	1.1	±	±	7.5	±	,,
3	S. L.	38 M	0.2	7.0	2 6	3.4	1.1	±	±	10.5	+	,,
4	B. R.	43 M	0.1	6.8	4.5	2.3	1.9	±	±	10.5	+	,,
5	D. D.	52 M	0.1	7.0	4.7	2.3	2.0	±	±	10.5	±	,,
6	K. K.	27 M	0.1	6.0	3.2	2.8	1 1	±	1+	5.0	∓	,,
7	M. S.	46 M	0.2	7.6	4.9	2 7	1.8	1+	1+	12.5	2+	,,
8	L. C	51 M	0.2	6.2	4.1	2.1	2.0	1+	1+	7.5	±	,,
9	C. S.	35 M	0.1	6.6	4.7	1.9	2.4	1+	1+	7.5	±	,,
10	K. C.	51 M	0.3	6.2	3.9	2.3	1.7	±	1+	10.5	±	,,
11	P. S.	25 M	0.1	5 7	3.8	2.9	1.3	—	±	7.5	—	,,
12	P. N.	50 M	0.2	7.2	4.2	3.0	1.4	1+	2+	12.5	2+	,,
13	K. S.	51 M	0.1	6.9	4.0	2.9	1.3	±	1+	10.5	±	,,
14	G. L.	45 M	0.2	7.2	5.1	2.1	2.4	±	1+	12.5	1+	,,
15	K. S.	42 M	0.1	6.4	3.5	2.9	1.2	—	±	5.0	—	,,
16	K. S.	60 M	0.2	7.0	4 0	3 0	1.3	—	±	5.0	—	,,
17	K. S.	44 M	0.2	6.6	3.7	2.9	1.3	—	∓	7.5	—	,,
18	R. S.	40 M	0.3	6.0	3.8	2.2	1.7	—	±	12.5	—	,,
19	C. N.	54 M	0.1	5.9	3.0	2.9	1.1	1+	2+	10.5	—	,,
20	K. R.	26 F	0.4	7.0	4.2	2.8	1.5	1+	2+	10.5	±	,,
21	G. D.	50 F	0.3	7.8	4.9	2.9	1.7	—	±	7.5	—	,,
22	K. K.	50 F	0.1	7.1	3.8	3.3	1.1	1+	2+	7.5	—	,,
23	M. D.	40 F	0.1	6.6	4.1	2.5	1.6	±	1+	10.5	1+	,,
24	K. V.	27 F	0.1	7.8	4.2	3 6	1.1	±	1+	10.5	2+	,,
25	I. K.	42 F	0.1	7.6	3.9	3.7	1.1	+	1+	12.5	±	,,
26	M. D.	32 F	0.2	7.0	4.1	2.9	1.4	1+	1+	7.5	±	,,
27	S. K.	45 F	0.2	7.1	3.9	3.2	1.2	1+	2+	10.5	±	,,
28	S. D.	50 F	0.2	6.8	3.8	3.0	1.3	—	—	5.0	—	,,
29	T. D.	45 F	0.1	7.0	3.5	3.5	1.0	1+	1+	7.5	—	,,
30	P. R.	50 F	0.1	6.8	4.0	2.8	1.4	—	—	7.5	—	,,
31	H. K.	43 F	0.1	6.6	3.5	3.1	1.1	±	±	5.0	—	,,
	Mean:—		0.16 ±0.01	6.57 ±0.1	4.0 ±0.09	2.5 ±0.12	1.44 ±0.07			5.8 ±1.01		

Table II

Comparative Values of Liver Function Tests in Essential Hypertension.
Total number of cases: 31.

Liver Function Test		No. of cases.
Total serum Bilirubin :		
	0.1 mg%	16
Upto	0.4 mg%	15
Total serum protein :		
	5 – 6 %	5
	6.1 – 6.5%	3
	6.6 – 7%	15
	Above 7%	8
Serum Albumin:		
	3 – 3.5%	6
	3.6 – 4%	13
	4.1 – 4.5%	7
	4.6 – 5%	4
	Above 5%	1
Serum Globulin :		
	Less than 2%	1
	2 – 2.5 %	7
	2.6 – 3%	15
	3.1 – 3.5%	6
	Above 3.5%	2
Thymol Turbidity in Maclagan Units :		
	Upto 5	6
	5 – 10.5	20
	10.6 – 12.5	5
Thymol Flocculation at 18 hours :		
	– ve	14
	±	12
	+	2
	++	3
Cephalin-Cholesterol Flocculation at 24 Hrs.		
	– ve	12
	±	9
	+	10
Cephalin-Cholesterol Flocculation at 48 hours :		
	– ve to ±	14
	+	12
	++	5

Table III

(of case No. 31)

Before onset of hepatitis.	After onset of hepatitis.		
Urine:			
Nothing abnormal.	Albumin	+	
	Bile salt	+	
	Bile pigment	+	
	Urobilinogen	+ve	1:20
X-ray heart: Enlarged.			
E. C. G. : Left ventricular strain.			
Plain X-ray, abdomen:			
Nothing abnormal.			
Intravenous Pyelography :			
Nothing abnormal.			
Fundus Examination :			
Grade III changes.	Grade III changes.		
Blood :			
Urea=32 mg%	Urea=28 mg%		
	Serum cholesterol=166 mg%		
	Serum Alkaline Phosphatase= 7.8 Bodansky units/100 c.c.		
	Prothrombin Index=84%		
	Hb=13. 0 Gm.		
	RBC=3.4 millions/cm.		
	TLC=8200/cm.		
	DLC=76/24/-/-		

Liver function tests on serum :

		20-8-56	3-9-56	19-9-56	28-9-56
Bilirubin in mg%:	0.1	8.0	3.3	20.0	40.0
Total Protein:	6.6	7.0	6.4	—	—
Albumin:	3.5	3.7	3.8	—	—
Globulin:	3.1	3.3	2.6	—	—
Thymol Turbidity in Maclagan units:	5	32	28	28	—
Thymol Flocculation at 18 hrs:	-ve	++	+	++	—
Cephalin-Cholesterol Flocculation (a) 24 hours:	+	++	++	++	—
(b) 48 hours:	+	++	++	++	—
Blood Pressure:	$\frac{220}{120}$ mm. of Hg.	$\frac{170-150}{110-95}$ mm. of Hg.			

this hepatic phase her blood pressure ranged betweed 150–170/90–110 mm. of Hg. She was not given any hypotensive drugs except for serpasil(0.25 mg) whenever blood pressure crossed 160,/100 and the patient felt somewhat restless.For the first 3 days in the hospital she improved under usual treatment of infective hepatitis but the temperature persisted, ranging from 100–102° F. On August 20, 1956, she passed into a state of semicoma and became delirious. Vigorous treatment was given but the coma gradually deepened. She was removed by her relations from the hospital against medical advice and 3 days later she expired. During the last days of her life the blood pressure ranged between 140–150/95–100mm. of Hg.

Here is a case in which the persistent high blood pressure reading fell as the liver failure advanced, thereby illustrating the dependance of essential hypertension on adequate hepatic function. This was the only case of essential hypertension in the series under reference, who later developed hepatitis.

We are still uncertain about the exact etiology of essential hypertension. Various theories and hypotheses have been expounded from time to time. Amongst others, plasma protein, belonging to alpha2 globulin fraction, the so-called hypertensinogen , has also been incriminated in the production and maintenance of hypertension (Braun-Menendez, et al, 1940. and Page, et al, 1947 as cited by Best and Taylor). It has been stated that the renin of the kidneys activates or transforms the inert hypertensinogen into the active form, hypertensin. In view of the vital role played by the liver in the synthesis of proteins, it is conceivable that a functionally active liver contributes this globulin which is essential for the maintenance of blood pressure ; and when the liver is damaged along with other functions it loses its ability to elaborate hypertensinogen. This would explain the fall in high blood pressure following acute liver disease as was observed in one of the cases under reference.

Serum albumin: globulin ratio in some of the cases under reference was found to be less than 1.5 and the slight variation of fractions from the normal range was associated with a disturbance in thymol turbidity test in a few of these hypertension cases. Whether this was due to "the presence of an abnormal globulin necessary for the persistence of essential hypertension" as suggested by Loyke (1955), has yet to be established.

SUMMARY

1. Liver function tests were performed on 31 cases of essential hypertension.
2. Liver function tests indicated a normal liver in most of the cases or a liver with a minimal damage in a few of the cases.

3. Established hypertension was found to be reversed to normal pressure with the onset of hepatic failure in one of the cases.

4. A shift from the normal albumin globulin, as seen in some of the cases of essential hypertension, is suggestive of the presence of an abnormal globulin.

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