

Autonomic Neuropathy in Cirrhosis

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SUMMARY

Autonomic nervous system involvement has been described in association with chronic liver disease. We studied 23 hospitalized patients with documented chronic liver disease 12 patients belonged to child C and rest of them belonged to Child class A or B. Two patients were HBsAg and anti HCV +ve, 16 were anti HCV +ve. Autonomic neuropathy was observed in 60% of the patients. Abnormalities were more marked in child C cirrhosis and parasympathetic function were more impaired as compared to sympathetic function.

DISCUSSION

INTRODUCTION

Hepatic dysfunction on its own irrespective of its etiology affects autonomic nervous system. Exact pathogenesis is unknown. The degree of autonomic dysfunction worsens with progression of liver disease. Generally parasympathetic nervous system is affected earlier and more than sympathetic nervous system. Autonomic dysfunction may be responsible for altered fluid homeostasis and neurohumoral disturbances in cirrhosis. A five fold increase in mortality has been observed in cirrhotics with autonomic dysfunction. Variceal bleeding and sepsis are the major causes of mortality.

AIMS

The aim of our study was to assess presence and degree of autonomic dysfunction in our cirrhotic population.

PATIENT AND METHODS

Twenty three patients with documented chronic liver disease admitted on the medical floor for various reasons i.e. work up, variceal bleeding, encephalopathy etc. were assessed.

Etiology and degree of hepatic dysfunction was worked up and patients were categorized into child A, B and C according to pugh's modified criteria.

We performed four tests of autonomic function. Sympathetic nervous system was assessed by recording postural change (lying to standing) in blood pressure. Postural change in heart rate which

is a function of parasympathetic nervous system was recorded as 30th beat after standing to 15th beat ratio.

Variation in heart rate with deep breathing for 6 cycles (each 10 sec) is also a function of parasympathetic nervous system. Mean heart rate variation for 6 cycles was calculated. Lastly valsalva maneuver was performed for 15 sec and valsalva ratio was calculated from minimum RR during valsalva to maximum RR interval after valsalva. This is also a function of parasympathetic nervous system.

RESULTS

Out of 23 patients 20 were male and three were female. their ages ranged from 40 to 75 years with a mean of 55 years (Table 1).

	Class C	Class B	Class A	Total
Table 1: Demographic data.				
Total patients	12	8	3	23
Male	10	6	4	20
Female	2	2	0	4
Mean age	54 ± 10.63			
Range	40-60			

Twenty one of the 23 belonged to child B or C (12 child C). Sixteen patients had hepatitis C 5 had hepatitis B and two were negative for both (Table 2).

None of the patients had significant postural drop in blood pressure 30:15 ratio was abnormal in 12 patients and all of them belonged to child B or C.

Seventeen patients had abnormal heart rate response to deep breathing and 16 of them belonged to child B or C (Tables 3, 4).

Table 2: Pugh-child classification.

	Number	Percent
Classification		
Class A	4	15.5
Class B	10	38.7
Class C	12	46.4
Serology		
HBV	6	23.6
HCV	20	77.1

Valsalva ratio was abnormal in 13 patients and 11 of them belonged to child B and C (Table 5).

On the whole 60% of the patients studied had two or more abnormal tests suggesting significant association between postnecrotic cirrhosis and autonomic neuropathy 90% of the patients in the autonomic dysfunction had advanced liver disease. Parasympathetic involvements was more than sympathetic involvement.

Table 3: 30:15 ratio.

	Value	No. of cases	Child pugh-classification		
			A	B	C
Abnormal	≤ 1.0	12	-	6	6
Borderline	1.01-1.03	6	-	-	-
Normal	≥ 1.01	8	8	-	-

Table 4: R-R variation with deep breathing.

	Rate variation	No. of cases	No. in child-pugh class		
			A	B	C
Abnormal	≤ 10 BPM	18	2	8	8
Borderline	11-14 BPM	4	1	-	-
Normal	≥ 15 BPM	6	6	-	-

Table 5: Valsalva ratio.

	Value	No. of cases	No. in child-pugh class		
			A	B	C
Abnormal	≤ 1.1	16	-	4	12
Borderline	1.11-1.2	4	-	4	-
Normal	≥ 1.21	6	4	2	-

DISCUSSION

Autonomic dysfunction has been described in association with chronic liver disease^{1,2}. Hepatic dysfunction on its own irrespective of the cause such as viral hepatitis, alcoholism, primary biliary cirrhosis affects ANS³. Exact pathogenesis is unknown³. Autonomic neuropathy worsens with progression of liver disease. Generally parasympathetic nervous systems is affected earlier and more than sympathetic nervous system ANS dysfunction may be responsible for altered fluid homeostasis and neuro humoral disturbances in cirrhosis^{1,2,3}. A five fold increase in mortality has been observed in those cirrhotic having ANS dysfunction - primarily due to variceal bleeding and infections³⁻⁵.

The aims of our study was to assess presence and degree of ANS dysfunction in our cirrhotic patients population. Twenty six patients with confirmed diagnosis of cirrhosis admitted in Shaikh Zayed Hospital for different reasons were assessed tests were performed in cooperative patients who have been stable hemodynamically for at least 48 hours. Patients with concomitant illnesses such as diabetes mellitus affecting ANS were excluded.

Postural change in BP is a function of sympathetic nervous system. Immediately after standing there is tachycardia which is maximum around 15th heart beat and then due to vagal discharge bradycardia which is maximum around 30th beat. 30:15 ratio is a test of parasympathetic nervous system. Continuous ECG recording was used during change of posture to calculate this ratio.

Variation in heart rate with deep breathing is also a function of parasympathetic nervous system. Patients while seated comfortably were asked to breath deeply with each phase lasting 5 sec. ECG

was recorded for six cycles and heart rate was calculated from shortest RR during inspiration and longest RR during expiration and then mean heart rate variation of 6 cycles with deep breathing was calculated.

Healthy patients were asked to perform Valsalva maneuver for 15 sec. while ECG was being recorded. Valsalva ratio was calculated from maximum RR interval after Valsalva to minimum RR interval during Valsalva. This is also a test of parasympathetic ANS.

Out of 26 patients 20 were male and 6 were female. Their ages ranged from 40-60 years with a mean age of 54 years.

Majority i.e. 84% of the patients had either child B or C disease. Twenty patients were (IgM + IgG) anti HCV positive while the rest had hepatitis B. None of the patients had a significant i.e. ≥ 10 mmHg postural drop in BP - sympathetic ANS.

Valsalva ratio was abnormal in 61% of the patients and 75% of these belonged to child B or C.

Sixty nine percent of the patients had abnormal heart rate response to deep breathing 90% of these belonged to child B or C.

30:15 ratio was abnormal in 46% of the patients and all of them belonged to child B or C.

On the whole 61% of the patients studied had (autonomic neuropathy i.e.) 2 or more abnormal tests - suggesting significant association between post necrotic cirrhosis and autonomic neuropathy. Eighty seven percent of the patients with autonomic neuropathy belonged to child B or C. Parasympathetic nervous systems was affected more than sympathetic NS^{6,7}.

CONCLUSIONS

1. Post hepatic chronic liver disease is associated with autonomic dysfunction.
2. Autonomic impairment is severe in advanced cirrhosis.
3. Parasympathetic nervous system is affected more than sympathetic nervous system.

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