



EVALUATION OF THE INVOLVEMENT OF AUTONOMIC NERVOUS SYSTEM IN PATIENTS OF CIRRHOSIS AND IT'S CORRELATION WITH ETIOLOGY

Medicine

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ABSTRACT

Introduction: Cirrhosis is among the top ten causes of death worldwide mostly due to alcohol abuse, chronic hepatitis, biliary diseases and iron over load. A wide range of functions are controlled by autonomic nervous system through sympathetic and parasympathetic nervous system. Explanation to increase death rate in cirrhosis not known but is possible that presence of autonomic neuropathy resulting defective response to stressful event.

Material & Methods: The study was carried out in patients of cirrhosis in Department of Medicine at N S C B Medical College & Hospital, Jabalpur after informed consent. The duration of study was one year and all simple, non invasive bedside tests of proven value were carried out to test autonomic dysfunction.

Results & Observations: Around 50% of patients were of age group of 40-55 year out of which 15 were male and 9 were female. History of alcoholism was present in 32% cases while 68% cases were non alcoholic. Out of 8 cases of alcohol related etiology 3 belonged to Child A and 5 belonged to Child B & C. In 17 cases of non-alcoholic cirrhosis 6 belonged to Child A and 11 belonged to Child B & C. Most affected test in alcoholic group were VR, E/I ratio, followed by atropine heart rate test. In Non alcoholic cirrhosis VR, E/I ratio and SHG were significantly abnormal.

Conclusions & Summary: This study concludes that autonomic dysfunction is quite common in cirrhosis mostly occurring in the later stage of cirrhosis irrespective of etiology of cirrhosis involving sympathetic and parasympathetic nervous system.

KEYWORDS

Cirrhosis, Autonomic Dysfunction, Valsalva Ratio, Sustained Hand Grip test,

Introduction

It was Laennec who in 1819 rather casually introduced the term cirrhosis in a footnote in his 'Traite' de l'Auscultation'; he regarded the granulations as neoformations, and because of their colour he called the condition in the liver 'cirrhosis', since 'kirros' in Greek means yellow or tawny.¹ Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end stage liver disease.² Cirrhosis is a major risk factor for the development of hepatocellular carcinoma and deaths from cirrhosis have been estimated to increase and would make it as the 12th leading cause of death in 2020.³ During 2001, the estimated worldwide mortality from cirrhosis was 771,000 people, ranking 14th and 10th as the leading cause of death in the world and in developed countries, respectively.⁴ The exact prevalence of cirrhosis worldwide is unknown. Cirrhosis prevalence was estimated at 0.15% or 400,000 in the USA, where it accounted for more than 25,000 deaths and 373,000 hospital discharges in 1998.²

The human internal environment is regulated in large measure by the autonomic nervous system and endocrine glands in an integrated manner. A wide range of functions of body are controlled by autonomic nervous system through the sympathetic, parasympathetic or both nervous systems. With the help of autonomic nervous system rapid changes are possible in the normal functioning of the different body functions and these capabilities help us to adapt to changes in the environment.

Autonomic dysfunction (AD) is an impairment of the normal functioning of the autonomic nervous system that adversely affects health. It can be primary or secondary, acute or chronic, and transient or progressive.⁵ The prevalence of AD in chronic liver disease is as high as 67% in some populations furthermore; the importance of autonomic dysfunction is highlighted by its associated increase in mortality.⁶ Chronic liver disease has been shown to be associated with autonomic neuropathy (AN) as well as hemodynamic and circulatory disturbances. This abnormality of the nervous system appears to be

unrelated to the toxic effects of chronic alcohol use, because cross-sectional studies have shown an equal prevalence of autonomic neuropathy in alcohol- and non-alcohol-related liver disease. Autonomic neuropathy is well described in diabetes mellitus, cerebrovascular disease, spinal cord lesions, and the Shy-Drager

syndrome as well as being associated with certain drugs.⁷ Alcoholism is also reported as a cause of autonomic neuropathy. Alcohol-induced brain damage and peripheral neuropathy have been recognized for more than a century. During the last decade autonomic neuropathy has also been reported in association with chronic alcohol abuse. The pathogenesis of this neuropathy is unknown but it has been suggested that it may be due to the toxic effect of alcohol on the nervous system.⁸ The factor most directly affected with the development of alcoholic neuropathy include the duration and amount of total lifetime consumption. Neuropathy is more prevalent in frequent heavy and continuous drinkers compared with more episodic drinkers.⁹ Explanation to increase death rate in cirrhosis not known but is possible that presence of autonomic neuropathy resulting defective response to stressful event. Hence this endeavours us to study patients of cirrhosis with special regards to autonomic function. Here our main concern is to study the autonomic dysfunction in cirrhotic patients with the help of simple non-invasive bedside tests.

Aim & Objectives: This study was taken with the aim to evaluate the involvement of autonomic nervous system in hepatic cirrhosis and to correlate between prevalence of autonomic nervous system dysfunction with age, duration and etiology of cirrhosis.

Material & Methods:

This study was carried out on 25 patient of cirrhosis taken from inpatient and outpatient department of Medicine of NSCB Medical College Hospital Jabalpur. The selection of patient was done randomly. Patients were labeled as case of cirrhosis when patient clinically had signs of liver cell failure and clinically decreased liver span with biochemical profile suggestive of chronic liver disease. The evidence of USG proof of liver cirrhosis is also included in the inclusion criteria. All the patients were on conservative line of management and any drug which affects autonomic function was stopped one week before testing. The control group was formed by age and sex matched healthy volunteers. Informed consent was obtained both from the patient and the control group. Simple, non-invasive bedside tests of proven value were carried out to test autonomic nervous dysfunction. All tests were done with patients supine unless indicated. The heart rate response was recorded with electrocardiograph recorder and blood pressure with an aneroid sphygmomanometer. All the subjects (patients and control group) were subjected to a battery of tests to evaluate entire reflex arc.

First deep breathing exercise was done for 1 minute followed by Valsalva maneuver, and sustained hand grip test. Following this the subjects and controls were made to stand from supine position for the orthostatic test. Lastly, they were made to lie down and 1.8 to 3.0 mg (0.04 mg/kg body weight) of atropine sulphate was injected intravenously for the atropine test. Clinical test performed for cardiovascular autonomic functions were Deep Breathing Exercise calculated by E.I ratio (E/IR), The Valsalva Maneuver calculated by Valsalva ratio (VR), Sustained Hand Grip Test (SHG), Orthostatic test calculated by 30:15 & Max-Min ratio and Intravenous Atropine test (Atropine heart rate test-AHRT). Data was analyzed using SPSS software. Significance level was $p < 0.05$.

Results & Observations:

64% cases were male where as 36% cases were females. The distribution of sex was similar between cirrhosis and control. The incidence of cirrhosis is low in female as alcoholism in one of the most common cause of cirrhosis in males.

Table-1: The distribution of cases in relation to etiology

AGE GROUPS	n	Alcoholic		Non-alcoholic	
		NO.	%	NO.	%
10-24	2	0	0	2	-
25-39	6	2	33.3	4	66.7
40-54	12	5	41.7	7	58.3
55-80	5	1	20	4	80
Total	25	8	32	17	68

Table-2: Classification of cases according to child grading with etiology of cirrhosis

Age group	Cases				Total		Control (Group III)	
	Child A (Group I)				Child B (Group II)			
	No.	%	No.	%	No.	%	No.	%
Alcoholic	3	37.5	5	62.5	8	32	0	0
Non alcoholic	6	18.8	11	34.4	17	68	15	100
Total	9	22.5	16	40	25	100	15	100

Table-3: Evaluation of autonomic function in patients with alcoholic Cirrhosis

S.No.	Tests	Alcoholic cirrhosis (n=8)					
		Normal		BL		Abnormal	
		No.	%	No.	%	No.	%
1.	E/IR	2	25	0	0	6	75
2.	VR	0	0	1	12.5	7	87
3.	30:15	5	62.5	0	0	3	37.5
4.	SHG	4	50	1	12.5	3	37.5
5.	AHRT	3	37.5	1	12.5	4	50
6.	ORT	5	62.5	2	20.1	1	12.5

Table: 4 Evaluation of autonomic function in patients with Non alcoholic Cirrhosis.

S. No.	Tests	Non-alcoholic cirrhosis (n=17)					
		Normal		BL		Abnormal	
		No.	%	No.	%	No.	%
1.	E/IR	6	35.3	0	0	11	64.7
2.	VR	2	11.8	2	11.8	13	76.5
3.	30:15	7	41.2	0	0	10	58.8
4.	SHG	8	47.06	1	5.88	8	47.06
5.	AHRT	7	41.2	3	17.6	7	41.2
6.	ORT	7	41.2	9	52	7	5.9

Discussion:

Cirrhosis is the major cause of morbidity and mortality in addition to enormous socioeconomic losses worldwide. The study comprised of 16 males and 9 females with age range of 15-80 years but maximum cases (68%) belonged to the age group of > 40 years. Patients were classified according to their liver function derangement and clinical profile (i.e. ascites, albumin, bilirubin) and CNS status in to child A and child B/C group to show severity of hepatocellular dysfunction. Nine (36%) patients belonged to child A and sixteen (84%) belonged to child B/C group. In Group-I (child-A) majority of patients were of non-

alcoholic etiology (six out of nine) while three belonged to alcoholic etiology. In Group-II (child B/C) majority of patients belonged to cirrhosis due to non-alcoholic etiology.

It was found that 23 out 25 cases showed evidence of autonomic dysfunction while all 25 controls had normal autonomic function. When autonomic functions were compared in patients with alcoholic and non alcoholic etiology it was found that seven cases with alcoholic etiology and 16 cases with non alcoholic etiology showed autonomic dysfunction. In a study conducted by Thuluvath P J et al forty-five per cent of patients with alcoholic liver disease and 43 per cent with non-alcoholic liver disease showed evidence of parasympathetic damage; 11 percent of patients with alcoholic liver disease and 12 per cent with non-alcoholic liver disease had sympathetic damage.⁷ In another study by Gentile et al autonomic dysfunctions was noted in 71% of cases with alcoholic etiology and in 57% cases with non alcoholic etiology.¹⁰ Another study conducted by Bajaj B K et al concluded that 90% of the alcoholics and 70% of the non-alcoholics had autonomic neuropathy.¹¹ Among the tests of parasympathetic system the most commonly affected test was Valsalva ratio (80%). Other tests like E/I ratio (68%), AHRT (44%) were also abnormal. Among the two tests of sympathetic involvement SHG was the most frequently affected test (44%). Dillon et al in their study noted that irrespective of etiology, there is a high prevalence of autonomic dysfunction in cirrhosis, and it is related to disease severity.¹² In a study by Khosla et al it was observed that Valsalva ratio was abnormal in 60% patients and 80% patients have evidence of autonomic neuropathy.¹³ In our study it was observed that 23 out 25 patients showed autonomic dysfunction. 3 patients (13.06%) showed sympathetic, 10 (43.47%) showed parasympathetic while 10 (43.47%) showed both system involvement. In our study autonomic dysfunction, in child group A patients seven were having autonomic dysfunction while two patients were normal. In child group B/C out of 16 patients not a single patient was normal. In present study 7(87.5%) of alcoholic and 16(94.12%) of non alcoholic had significant autonomic dysfunctions. Valsalva ratio was abnormal in 80% patients and inconclusive in 12%. In a study by Mac Gilchrist et al in 29 patients and 20 controls significant reduction in Valsalva ratio was observed.¹⁴ The results of this study give some idea about autonomic dysfunction in cirrhosis. However, long term follow up and a study with larger population of cirrhosis is required for analyzing the mortality and morbidity of autonomic involvement in cirrhosis.

Conclusions:

Present study concludes that autonomic dysfunctions are quite common in cirrhosis which mostly occurs in later stages of cirrhosis. Autonomic dysfunctions occur in alcoholics and non alcoholics irrespective of etiology. Both parasympathetic and sympathetic systems are involved, however parasympathetic system is more commonly involved.

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