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RESEARCH ARTICLE

SODIUM AND CALCIUM LEVELS IN PATIENTS WITH CIRRHOSIS OF THE LIVER AND ITS CORRELATION WITH HEPATIC ENCEPHALOPATHY

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Abstract

Introduction: Patients with chronic liver disease have a specific susceptibility to an electrolyte imbalance that can deteriorate their condition to hepatic encephalopathy. It occursin about 57% of hospitalized patients with cirrhosis. Hyponatremia in cirrhosis is an in dependent risk factor for mortality and is common in patients with end-stage liver disease. These patients had a significantly higher incidence of hepatic encephalopathy, hepatorenal syndrome, and spontaneous bacterial peritonitis. Hepatic encephalopathy is worsened by the presence of hyponatremia and hypocalcemia.

Aim: The aim of this study is to evaluate sodium and calcium levels in CLD patients and its correlation with hepatic encephalopathy.

Methods: This cross-sectional study was conducted in SMHS Hospital,Govt.Medical College Srinagar, Jammu Kashmir,India, during a three-year period. 150 patients with chronic liver disease admitted to the general medicine and gastroenterology department were included. Data was entered in SPSS software version 20. Qualitative data were analyzed using chi-square, and quantitative data were analyzed using independent t-tests. A P-value <0.05 was considered significant.

Results: Our study on 150 CLD patients showed that the serum sodium level and serum calcium level were significantly lower in patients with hepatic encephalopathy with P-Values of 0.0006 and 0.002, respectively.

Conclusion: It seems that reducing serum sodium and calcium level can be predictive of hepatic encephalopathy inpatients with chronic liver disease.

Introduction:-

Cirrhosis is a pathologically defined entity that is associated with a spectrum of characteristic clinical manifestations. The cardinal pathologic features reflect irreversible chronic injury of the hepatic parenchyma and extensive fibrosis in association with the formation of regenerative nodules. Hepatic encephalopathy (HE) is a neurometabolic syndrome characterized by impaired brain function in patients with decompensated cirrhosis.[1-3] The pathogenesis of HE is not completely understood and several proposed pathways are implicated in the initiation and exacerbation of this syndrome.[3,4] Ammonia plays a central role in HE as it crosses the blood brain barrier causing neurological insultmediated by a decrease in excitatory neurotransmission.[3-5] Multiple precipitating factors for HE has been recognized and if controlled, may alter the disease activity and improve mental status.[6] The most common

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precipitating factors for HE includes dehydration, acute kidney injury,non-adherence to medications (particularlynon-absorbable disaccharides), constipation, and infections.[7-9] HE is associated with a mortality risk of up to 54%in the first 12 months of initial presentation.[10,11] Many patientswith acute HE requires hospitalization and intensivecare unit (ICU) admission, which may be associated withworse outcomes. Fichet and colleagues studied the prognosis and one-year mortality in patients with HE and found that arterial hypotension, mechanical ventilation, vasopressor use, acute renal failure, and sepsis were among the most common factors associated with mortality in the ICU.[10] Another study found that diabetes melitus, hypertension,prior trans-jugular intrahepatic portosystemic shunt (TIPS) placement, prior HE, and prior use of lactulose were associated with increased 90-day readmissionrates.

Serum electrolyte derangements are common in patients with decompensated cirrhosis hospitalized for hepatic encephalopathy. There are limited data describing the association between electrolyte levels and outcomes in hepatic encephalopathy.We assessed the association between initial serum electrolyte values(sodium and calcium) and outcomes in patients with hepatic encephalopathy.

Materials And Methods:-

Study setting

This study was carried out at the inpatient department of medicine and gastroenterology in a tertiary care hospital in Jammu Kashmir, India.

Subjects, sample size, and sampling technique

A total of 150 patients of both genders with hepatic cirrhosis were approached. Simple random sampling was performed.

Study design

The research approach employed a cross-sectional study design to correlate electrolyte abnormalities with HE in patients with liver cirrhosis.

Inclusion and exclusion criteria

Patients with diagnosed hepatic cirrhosis of any etiology who were aged between 18-80 years were included in this study. Patients under treatment for hepatocellular carcinoma, ascites, and hyponatremia,hypocalcemia were excluded. Patients with underlying renal pathology, those on dialysis, and patients on diuretic therapy were also excluded.

Data collection procedure

After obtaining approval from the ethical committee of the hospital, the study was carried out in the inpatient department of internal medicine and gastroenterology. All the patients were informed about the nature of the study and their verbal consent was obtained. After taking relevant history and physical examination, the venous blood sample of each patient was drawn and sent to the institutional laboratory for estimation of serum electrolytes, liver function tests (LFTs), renal function test, prothrombin time (PT), and international normalized ratio (INR). We classified the HE according to the West Haven classification system. Mild to moderate encephalopathy was classified under grades I-II, whilesevere encephalopathy was classified under grades III-IV. We documented the severity of liver diseaseaccording to the Child-Pugh score criteria. The patients were classified into different groups based on the serum sodium concentration as follows: level of <130 meql/l (significant/severe hyponatremia), between 131and 135 meq/l (mild hyponatremia), and level of >135 meq/l (normal). A specialized proforma was designed to collect all the study information.

Data analysis

All data were analyzed using SPSS Statistics version 20. We reported the data as means along with standard error. Qualitative data wereanalyzed using the chi-square test and quantitative data was analyzed using an independent t-test. A p-value of <0.05 was considered statistically significant. Conclusions were drawn accordingly.

Results And Observations:-

Table 1:- Hyponatremia and its correlation with hepatic encephalopathy.

Hyponatremia	Hepatic encephalopathy	Total	Significance

	Present	Absent		
Yes	42	23	65	P=<0.0001
No	12	73	85	
Total	54	96	150	

Table 2:- Mean serum sodium and its correlation with hepatic encephalopathy.

	With encephalopathy	Without encephalopathy	Total	P value
Mean serum sodium	131.9±7.91	135.5±4.64	134.2±6.24	0.0006

Table 3:- Correlation of severity of hyponatremia with grades of hepatic encephalopathy.

Severity of hyponatremia	Grades of hepatic encephalopathy					Significance
	1	**2**	**3**	**4**	**None**	
Mild	11	5	3	2	24	P=<0.0001
Moderate	2	4	6	4	0	
Severe	1	1	1	1	0	
None	9	1	2	1	72	
Total	23	11	12	8	96	

Table 4:- Correlation of Hypocalcemia with hepatic encephalopathy.

Hypocalcemia	Hepatic encephalopathy		Total	Significance
	Present	**Absent**		
Yes	38	9	47	P<0.0001
No	16	87	103	
Total	54	96	150	

Table 5:- Mean serum calcium level and its correlation with hepatic encephalopathy.

	With encephalopathy	Without encephalopathy	Total	p-value
Serum calcium	8.76±0.49	9.05±0.57	8.94±0.56	0.002

Table 6:- Correlation of severity of hypocalcemia with grades of hepatic encephalopathy.

Sr. calcium	Hepatic encephalopathy present				Hepatic encephalopathy absent	Significance
	Grade 1	Grade 2	Grade 3	Grade 4	None	
10-10.5	2	0	0	0	3	P value=0.0043
9.5-9.9	1	1	0	0	24	
9-9.4	3	5	2	2	31	
8.5-8.9	2	6	8	7	18	
8-8.4	2	3	4	6	20	
Total	**10**	**15**	**14**	**15**	**96**	

Among the patients, there were 95(63.3%) males and 55 (36.7%) females; the mean age of the patients was 62.16+13.93 years. Overall, serum sodium levels among the subjects ranged from 114 to148meq/L, with a mean of 134.2±6.24meq/L. In patients with hepatic encephalopathy, the mean sodium level was significantly lower(131.9±7.91meq/L) compared to patients without hepatic encephalopathy(135.5±4.64) with P=0.0006.

Hyponatremia was present in 65 (43.3%) patients. Among these, 45 (30%) patients had mild hyponatremia, 16 (10.6%) had moderate, and 4 (2.6%) had severe hyponatremia.Hepatic encephalopathy was present in 54 (36%) patients. Hepatic encephalopathy grade I was present in 23 (15.3%), grade II in 11 (7.3%), grade IIIin 12 (8%), and grade IV in 8(5.4%) patients. In 66 patients with hyponatremia, 54 were found to have HE.

In our study Serum calcium level was significantly lower in patients with hepatic encephalopathy(8.76±0.49meq/L) compared to the patients without hepatic encephalopathy(9.05±0.57meq/L)with P=0.002.

Hypocalcemia(serum calcium <8.8meq/L) was present in 47(31.3%)patients. Among them 38(25.3%) hepatic encephalopathy.

Discussion:-

Our study on 150 CLD patients showed that in the patients with hepatic encephalopathy, the serum sodium level and serum calcium level were significantly lower than those in the patients without hepatic encephalopathy. Our study showed a significantly lower level of serum sodium in encephalopathic groups. So, low serum sodium levels can be a risk factor for triggering hepatic encephalopathy.Hyponatremia in patients with CLD can cause a variety of manifestations. Hyponatremia can lead to mild cerebral edema, which results in increased osmotic pressure on astrocytes. Eventually, it leads to many neurological dysfunctions.

Our results are consistent with those of previous studies. In a study by Khalil et al., it was shown that the prevalence ofhyponatremia (serum sodium level of <130 meq/L) was 45.5% among the cohort, with a mean of 123.26 ±5.57 meq/L[12]. In another study,the prevalence of hyponatremia was found to be 30% [13]. A study done by Jenq et al. revealed that cirrhotic patients with hyponatremia had a higher in-hospital mortality rate[14].

A study by Lars Bossen et al. showed the hazard rate of hepatic encephalopathy development increased by 8% for every one mmol/L decrease in serum sodium[15]. Also sodium levels of <130 meq/L were associated with higher morbidity and mortality rates in other studies, showing that the patients with lower levels of sodium had higher grades of hepatic encephalopathy[16-20]. In some studies such as the one by Zheng Ning et al., it is reported that higher serum Sodium concentrations were significantly associated with the in-hospital mortality of CLD patients[24] , which is contrary to our findings in the study.

The association between hepatic encephalopathy and hyponatremia may be explained based on the higher severity of liver disease among patients with hyponatremia. On the other hand, the very nature of CLD by activating the effective volume of arteries activates the renin-angiotensin system and retains water and sodium. Therefore, it appears that with proper treatment of water and electrolytes and regular and periodic checking of electrolytes in patients, we can reduce the effect of this factor on exacerbating hepatic encephalopathy.

Serum calcium level was significantly lower in patients with hepatic encephalopathy compared to the patients without hepatic encephalopathy in our study. Hypocalcaemia can occur in patients with CLD due to vitamin D-dependent metabolism. In both parenchymal and cholestasis liver diseases, intestinal fat malabsorption may cause vitamin D deficiency, resulting in hypocalcemia. Also, it is necessary to mention that hypoalbuminemia due to liver dysfunction can result in a lower serum calcium level in CLD. In studies by Devaraj[21] and Schafer AL[22], similar to our study, hypocalcemia was found to be a predictive factor for hepatic encephalopathy.

The mortality rate among patients with hepatic encephalopathy was between 27-75% in various studies[23]. The overall mortality rate in our study was 30 (35.3%), of which 20 (60.6%) were in the group with hepatic encephalopathy. It is predictable due to the higher severity of CLD among patients with hepatic encephalopathy.

We evaluated that the electrolyte disturbance in CLD patients with and without hepatic encephalopathy as the timely identification, management, and treatment of predisposing factors for hepatic encephalopathy will play an essential role in reducing mortality in CLD.

Limitations of the study

Our study had some limitations which may affect the interpretation of our results includingthe single-center design and the inclusion of a small number of patients. Therefore, wesuggest multicentre studies with larger sample sizes for future research.

Conclusion:-

It seems that the decrease in serum sodium and calcium levelscan be predictive of hepatic encephalopathy in CLD patients.

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