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Original Research

Biochemical evaluation of serum sodium levels in patients with cirrhosis of liver

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ABSTRACT:

Background: To evaluate serum sodium levels in subjects with cirrhosis of liver. **Materials & methods:** A total of 50 subjects were enrolled. The subjects were divided into 2 groups cirrhosis group and control group as 25 in each. The results were analysed using SPSS software. The p- value less than 0.005 was considered significant. **Results:** A total of 50 subjects were enrolled. The mean age in subjects with serum sodium levels ≤130 mmol/L was 54.5 years and with 131-135 mmol/L concentration was 49.6 years **Conclusion:** Lower serum sodium levels were associated with cirrhosis of liver.

Keywords: cirrhosis, sodium, liver.

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INTRODUCTION

Hyponatremia is the most common electrolyte abnormality observed in hospitalized patients.[1] Hyponatremia in cirrhosis is currently defined as a serum sodium level of less than 130 meq/L. [2] It has been suggested that the prevalence of a serum sodium concentration less than 135, 130 and 120 meq/L in patients with cirrhosis and ascites is 49.4%, 21.6% and 1.2%, respectively. [3]Reduced serum sodium concentration is a common finding in patients with cirrhosis, being the most common electrolyte disorder in this setting.[4,5]Indeed, about 20% of patients have values lower than 130 mmol/L, which is the current definition of hyponatremia in cirrhosis.[6] However, even though patients with cirrhosis and serum sodium concentration between 130 and the lower normal limit of 135 mmol/L could not be considered as hyponatremic according to this definition, they present pathogenic and clinical features similar to those with serum sodium lower than 130 mmol/L. With the cutoff of 135 mmol/L, the prevalence of hyponatremia rises to almost 50%. Instead, the occurrence of severe hyponatremia, that is serum sodium concentration lower than 126 mmol/L, is rare and its prevalence is 6%. [5]

Hyponatremia is associated with a broad variety of neurological manifestations, whose intensity is related not only to the extent of serum sodium reduction, but also, and mainly, to the rate of fall. In fact, patients with acute hyponatremia have a much higher incidence of neurological symptoms than patients with chronic hyponatremia. [6] In patients without liver disease, the clinical effects of hyponatremia are related to brain edema, such as headache, disorientation, confusion, focal neurological deficits, seizures, and, in some cases, death due to cerebral herniation. [7] Moreover, hyponatremia leads to substantial changes in the brain intracellular environment to limit intracellular hyperhydration. These defense mechanisms consist of a rapid release of intracellular electrolytes, particularly potassium, which occurs within 24 h; subsequently, low-molecular-weight organic compounds, particularly myoinositol, are also discharged/released. [7]

The quality of life is poor in patients with cirrhosis and hyponatremia due to the requirement for strict fluid restriction. Hyponatremia has been found to be an independent predictive factor of the impaired health related quality life as well as hepatic encephalopathy.[8] Numerous studies have shown that the severity of hyponatremia and ascites is a major

determinant of disease severity and prognosis in cirrhosis.[9,10] In one study, the serum sodium level before the onset of spontaneous bacterial peritonitis (SBP) was an independent predictor of renal failure triggered by SBP.[11] It has also been suggested that serum sodium is an earlier and more sensitive test than serum creatinine to detect circulatory dysfunction resulting in renal failure and/or death.[12] Although patients with hyponatremia are at a very high risk for developing hepatorenal syndrome, low serum sodium in hepatorenal syndrome is not only due to high ADH levels but also due to decreased GFR and proximal sodium reabsorption. [13] Hence, this study was conducted to evaluate the serum sodium levels in subjects with cirrhosis of liver.

MATERIALS & METHODS

A total of 50 subjects were enrolled. The subjects were divided into 2 groups cirrhosis group and control group as 25 in each. The age group included was 45 to 60 years. Complete history was taken. Laboratory investigations were done. The data was collected. The results were analysed using SPSS software. The p-value less than 0.005 was considered significant.

RESULTS

A total of 50 subjects were enrolled. The mean age in subjects with serum sodium levels ≤130 mmol/L was 54.5 years and with 131-135 mmol/L concentration was 49.6 years. The p- value was 0.1. The control group had a serum sodium concentration as ≥136 mmol/L whereas, the subjects with cirrhosis had concentration ≤130 mmol/L and 131-135 mmol/L.

Table 1: Characteristics of patients according to serum sodium concentration

Characteristics	≤130 mmol/L	131-135 mmol/L	≥136 mmol/L	P- value
Gender				
Male	5	12	15	0.5
Female	3	5	10	
Age (years)	54.5	49.6	52.4	0.1

Table 2: serum sodium levels

Serum sodium levels	Control group	Cirrhotic group	P – value
≤130 mmol/L	0	8	0.001
131-135 mmol/L	0	17	
≥136 mmol/L	25	0	

The mean serum sodium levels in control group were 143.5 mmol/L and in cirrhosis group were 131.7 mmol/L.

Table 3: mean serum sodium concentration

Groups	Mean concentration (mmol/L)
Control group	143.5
Cirrhosis group	131.7

DISCUSSION

Although hyponatremia can be found in patients with early or moderately advanced cirrhosis belonging to classes A and B of Child-Pugh classification,[14] in most cases it occurs in an advanced disease (Child-Pugh class C). The relationship between hyponatremia and severity of cirrhosis is further evidenced by its close association with the occurrence of complications: indeed, the prevalence of hepatic encephalopathy, hepatorenal syndrome and spontaneous bacterial peritonitis is substantially higher in patients with serum sodium concentration ≤130 mmol/L than in those with higher levels. Moreover, among patients with ascites, those with hyponatremia have a lower response to diuretics, a higher incidence of refractory ascites, and more often need therapeutic paracentesis at shorter intervals. [3]Hence, this study was conducted to evaluate the serum sodium levels in subjects with cirrhosis of liver.

In the present study, a total of 50 subjects were enrolled. The mean age in subjects with serum sodium levels ≤130 mmol/L was 54.5 years and with 131-135 mmol/L concentration was 49.6 years. The p- value was 0.1.A study by Kim JH et al, showed the prevalence of dilutional hyponatremia, classified as serum sodium concentrations of <or=135 mmol/L, <or=130 mmol/L, and <or=125 mmol/L, were 20.8%, 14.9%, and 12.2%, respectively. The serum sodium level was strongly associated with the severity of liver function impairment as assessed by Child-Pugh and MELD scores (p<0.0001). Even a mild hyponatremia with a serum sodium concentration of 131-135 mmol/L was associated with severe complications. Sodium levels less than 130 mmol/L indicated the existence of massive ascites (OR, 2.685; CI, 1.316-5.477; p=0.007), grade III or higher hepatic encephalopathy (OR, 5.891; CI, 1.490-23.300; p=0.011), spontaneous bacterial peritonitis (OR, 2.562; CI, 1.162-5.653; p=0.020), and hepatic hydrothorax (OR, 5.723; CI, 1.889-17.336; p=0.002). Hyponatremia, especially serum levels <or=130 mmol/L, may indicate the existence of severe complications associated with liver cirrhosis. [15]

In the present study,the control group had a serum sodium concentration as ≥136 mmol/L whereas, the subjects with cirrhosis had concentration ≤130

mmol/L and 131-135 mmol/L.The mean serum sodium levels in control group were 143.5 mmol/L and in cirrhosis group were 131.7 mmol/L. Another study byJenq Cc et al, analyzed the outcomes of critically ill cirrhotic patients and identified the prognostic value of serum sodium concentration.One hundred twenty-six consecutive cirrhotic patients admitted to the ICU of a tertiary center during a 1.5-year period were enrolled in this study. Demographic, clinical, and laboratory variables on the first day of ICU admission were prospectively recorded for post hoc analysis. Overall hospital mortality was 65.1%. Comparing with serum sodium >135 mmol/L, patients with serum sodium <or=135 mmol/L had a greater frequency of ascites, illness severity scores, hepatic encephalopathy, sepsis, renal failure, and in-hospital mortality (55.9% vs. 73.1%, P=0.043). Multiple Cox proportional hazards analysis revealed that serum sodium levels, hepatocellular carcinoma, and sequential organ failure assessment scores on the first day of ICU admission were independent risk factors for 6-month mortality. Cumulative survival rates at 6-month follow-up after hospital discharge differed significantly (P<0.05) between patients with serum sodium >135 mmol/L versus those with serum sodium <or=135 mmol/L.Low serum sodium levels in critically ill cirrhotic patients are associated with high complications of liver cirrhosis, in-hospital mortality, and poor short-term prognosis. The serum sodium concentration is important predictor of survival among candidates for liver transplantation. Future research with sequential application of serum sodium may reflect the dynamic aspects of clinical conditions, thus providing complete data for mortality risk.[16] John S et al, studied that hyponatremia is frequently seen in patients with ascites secondary to advanced cirrhosis and portal hypertension. The development of ascites in patients with cirrhosis is multi-factorial. Portal hypertension and the associated systemic vasodilation lead to activation of the sodium-retaining neurohumoral mechanisms which include the renin-angiotensin-aldosterone system, sympathetic nervous system and antidiuretic hormone (ADH). The net effect is the avid retention of sodium and water to compensate for the low effective circulatory volume resulting in the development of ascites. Although not apparent in the early stages of cirrhosis, the progression of cirrhosis and ascites leads to impairment of the kidneys to eliminate solute- free water. This leads to additional compensatory mechanisms including non-osmotic secretion of ADH, also known as arginine vasopressin, further worsening excess water retention and thereby hyponatremia. Hyponatremia is associated with increased morbidity and mortality in patients with cirrhosis, and is an important prognostic marker both before and after liver transplant. The management of hyponatremia in this setting is a challenge as conventional therapy for hyponatremia including fluid restriction and loop diuretics are frequently inefficacious. In the review, they discussed the pathophysiology and various treatment modalities, including selective vasopressin receptor antagonists, for the management of hyponatremia in patients with cirrhosis.[17] Bernardi M et al, hyponatremia is common in cirrhosis. It mostly occurs in an advanced stage of the disease and is associated with complications and increased mortality. Either hypovolemic or, more commonly, hypervolemic hyponatremia can be seen in cirrhosis. Impaired renal sodium handling due to renal hypoperfusion and increased arginine-vasopressin secretion secondary to reduced effective volemia due to peripheral arterial vasodilation represent the main mechanisms leading to dilutional hyponatremia in this setting. Patients with cirrhosis usually develop slowly progressing hyponatremia. In different clinical contexts, it is associated with neurological manifestations due to increased brain water content, where the intensity is often magnified by concomitant hyperammonemia leading to hepatic encephalopathy. Severe hyponatremia requiring hypertonic saline infusion is rare in cirrhosis. The management of asymptomatic or mildly symptomatic hyponatremia mainly rely on the identification and treatment of precipitating factors. However, sustained resolution of hyponatremia is often difficult to achieve. V2 receptor blockade by Vaptans is certainly effective, but their long-term safety, especially when associated to diuretics given to control ascites, has not been established as yet. As in other conditions, a rapid correction of long-standing hyponatremia can lead to irreversible brain damage. The liver transplant setting represents a condition at high risk for the occurrence of such complications.[18]

Hyponatremia is associated with a broad variety of neurological manifestations, whose intensity is related not only to the extent of serum sodium reduction, but also, and mainly, to the rate of fall. In fact, patients with acute hyponatremia have a much higher incidence of neurological symptoms than patients with chronic hyponatremia.[6]In patients without liver disease, the clinical effects of hyponatremia are related to brain edema, such as headache, disorientation, confusion, focal neurological deficits, seizures, and, in some cases, death due to cerebral herniation. [8] Moreover, hyponatremia leads to substantial changes in the brain intracellular environment to limit intracellular hyperhydration. These defense mechanisms consist of a rapid release of intracellular electrolytes, particularly potassium, which occurs within 24 h; subsequently, low-molecular-weight organic compounds, particularly myoinositol, are also discharged/released.[8] These changes require time to be reverted. Thus, a rapid increase in serum sodium concentration would overcome cell adaptation and brain shrinkage may ensue. This would trigger demyelination of pontine and extrapontine neurons that can cause neurologic dysfunction, including quadriplegia, pseudobulbar palsy, seizures, coma, and even death. Interestingly, in

addition to malnutrition, potassium depletion, alcohol abuse, and hypocorticism, the risk of these complications is enhanced by liver cirrhosis. [8]Prevention of hypovolemic hyponatremia mainly consists in avoiding marked fluid losses in excess of sodium. The most frequent cause of hypovolemic hyponatremia in patients with cirrhosis and ascites is represented by diuretic overtreatment. Therefore, great care has to be paid in avoiding a markedly negative fluid balance. In practice, daily body weight reduction under diuretic treatment should not exceed 500–800 g.[19] Patients with peripheral edema appear to be protected from these effects because of the preferential mobilization of edema and may safely undergo diuresis at a more rapid rate (up to 2 kg/day) until edema disappear. [19]

CONCLUSION

Lower serum sodium levels were associated with cirrhosis of liver.

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