The Association Between the Serum Sodium Level and the Severity of Complications in Liver Cirrhosis

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Background/Aims: Dilutional hyponatremia associated with liver cirrhosis is caused by impaired free water clearance. Several studies have shown that serum sodium levels correlate with survival in cirrhotic patients. Little is known, however, regarding the relationship between the degree of dilutional hyponatremia and development of cirrhotic complications. The aim of this study was to evaluate the association between the serum sodium level and the severity of complications in liver cirrhosis.

Methods: Data of inpatients with cirrhotic complications were collected retrospectively. The serum sodium levels and severity of complications of 188 inpatients were analyzed.

Results: The prevalence of dilutional hyponatremia, classified as serum sodium concentrations of ≤135 mmol/L, ≤130 mmol/L, and ≤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).

Conclusions: Hyponatremia, especially serum levels ≤130 mmol/L, may indicate the existence of severe complications associated with liver cirrhosis. (Korean J Intern Med 2009;24:106-112)

Keywords: Hyponatremia; Liver cirrhosis

INTRODUCTION

Intractable ascites, severe hyponatremia, and decreased arterial pressure are clinical findings seen in patients with advanced cirrhosis. These conditions occur as a result of high serum levels of renin/aldosterone owing to portal hypertension, a decreased vascular response to vasoactive drugs, and a reduced solute-free water clearance [1-4]. According to several recent studies, hyponatremia occurring as a result of a reduced solute-free water clearance was a key prognostic factor in patients with liver cirrhosis when hyponatremia was incorporated into the MELD score [5-9]. Hyponatremia is a common abnormal finding in approximately 57% of hospitalized patients with chronic liver disease and in 40% of outpatients with liver disease [1,10]. To date, no studies have been conducted to evaluate the prevalence of hyponatremia in Korean hospitalized patients with liver cirrhosis. In fact, no studies have evaluated the association between serum sodium levels and the occurrence and severity of complications due to liver cirrhosis. Given the need for further studies regarding this relationship, we conducted this study to...
evaluate the prevalence of hyponatremia, to examine whether serum sodium levels correlate with the presence and severity of cirrhotic complications, and to estimate survival rates in patients hospitalized with complications due to liver cirrhosis.

**METHODS**

**Subjects**

Patients who were hospitalized with complications due to liver cirrhosis during a 1-year period between 1 January and 31 December 2004 at Ilsan Paik Hospital of Inje University, Korea were included in this study, if a retrospective chart analysis and follow-up telephone call were obtainable. For patient was admitted more than twice during the study period, the medical record of the first admission was collected. A diagnosis of liver cirrhosis was limited to cases with laboratory and clinical findings that met the proper diagnostic criteria [11]. Patients with hepatocellular carcinoma present at admission and during the follow-up period were excluded. Patients using diuretics within a 1-month period before admission and antiviral drugs at any time of survival period were also excluded from the current study. As causative factors for liver cirrhosis, chronic hepatitis B was diagnosed in cases with detectable hepatitis B surface antigen, and chronic hepatitis C was diagnosed in patients positive for anti-HCV antibody. Patients who had ingested alcohol daily at a dose of >80 g for more than 10 years in the absence of other causative factors such as drugs or evidence of a viral infection were defined as having alcoholic liver cirrhosis. Other cases were classified as ‘others’.

**Study design**

Based on the serum sodium concentration measured at the time of admission, patients were divided into three groups: serum sodium ≤130 mmol/L, serum sodium between 131 and 135 mmol/L, and serum sodium ≥136 mmol/L. Complications included simple ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatic hydrothorax, infection, hepatorenal syndrome, esophageal and gastric varices, upper gastrointestinal bleeding due to varices, and intractable ascites. Ascites, hepatic encephalopathies, and esophageal varices were classified based on severity. Ascites was classified as follows: grade I, ascites observed on imaging study but presence is unclear on physical examination; grade II, ascites easily recognized on gross examination and palpation; and grade III, severe abdominal distention concurrently present on gross examination and large-volume paracentesis performed for therapeutic purposes [12]. Cases of hepatic encephalopathy higher than grade III based on the West Haven criteria were determined to be severe, and other cases were all determined to be mild [13]. Presence of varix was described only the case endoscopic exam was done between 3 month before and after hospitalization. Esophageal varices were classified by size and shape based on endoscopic findings, as follows: F1, a linear, small sized varix, F2, a beaded, medium sized varix, and F3, a nodular, large varix [14]. Infection was defined in patients hospitalized with infectious diseases except for spontaneous bacterial peritonitis. In cases of hepatic hydrothorax and gastric varices, only the presence of such complications was verified. The concurrent presence of other complications was also examined in accordance with the treatment guidelines of the Korean Association for the Study of the Liver [15]. When death was confirmed on a retrospective analysis of medical records and a telephone interview, the period ranging from the date of hospitalization to death was considered as the survival period.

**Statistical analysis**

Statistical analysis was performed using SAS. Statistical methods included the Chi-square test and ANOVA. A p value <0.05 was considered statistically significant. To obtain the distribution curve for the survival time depending on the serum sodium concentration at the time of admission, an estimated value of Kaplan-Meier was calculated, and differences in survival time were analyzed using the log-rank test. A hazard ratio for the concurrent presence of complications depending on the severity of hyponatremia was obtained using logistic regression analysis.

**RESULTS**

**Patient characteristics**

In the current study, we analyzed 188 inpatients with liver cirrhosis who were hospitalized with complications such as simple ascites, spontaneous bacterial peritonitis, intractable ascites, hepatorenal syndrome, hepatic encephalopathy, variceal bleeding, hepatic hydrothorax, and infection. Patients in our series had a mean age of