Serum Zinc Levels in Hepatic Encephalopathy

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Abstract

Background: Zinc is essential for various metabolic processes of the body. Since serum zinc levels are lowered in liver diseases, it has been postulated to be a precipitating factor for hepatic encephalopathy.

Methods: We prospectively studied serum zinc levels in consecutive patients with fulminant hepatic failure, subacute hepatic failure and chronic liver disease with encephalopathy. Serum zinc levels were correlated with various clinical and biochemical parameters and final outcome of patients. Serum zinc levels were estimated by atomic absorption spectrometry at admission and also 24 hours after recovery in survivors.

Results: Of the 55 patients (age 17-65 years, 35 men) studied, 30 had acute, 5 subacute and 20 chronic liver disease. Patients with hepatic encephalopathy had significantly lower serum zinc levels as compared to 20 age and sex matched controls. High serum bilirubin levels and prothrombin time showed inverse relationship with serum zinc levels. There was no relationship of serum zinc levels with age, sex, grade and duration of encephalopathy, liver size, ascites or splenomegaly.

Conclusions: Hepatic encephalopathy is associated with low serum zinc levels. Recovery occurred in 17 patients despite persisting low serum zinc levels. Serum bilirubin >23 mg/dL and prothrombin time prolongation >12 seconds above control have inverse correlation with serum zinc level.

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Introduction

Zinc is an essential trace element since is constituent of a variety of metallo-enzyme systems and biochemical pathways in the metabolism of carbohydrates, fats and proteins. Its zinc deficiency is known to induce neurological and psychiatric symptoms including ataxia, lethargy, depression and hallucinations. In patients with liver disease, serum zinc levels are low. Zinc deficiency precipitates hepatic encephalopathy and zinc supplements improve mild chronic hepatic encephalopathy as measured by psychometric testing. In patients with fulminant hepatic failure, serum zinc levels were reported to increase after recovery. We therefore compared serum zinc levels in patients with hepatic encephalopathy with those in healthy controls and correlated serum zinc levels with clinical features and outcome of hepatic encephalopathy.

Methods

Fifty five consecutive patients (35 men, 20 women; aged 38.7±12.2 yr) with hepatic encephalopathy hospitalized over one-year period were included in the study. Patients suffering from other diseases known to affect serum zinc levels like chronic renal failure and diabetes mellitus and those receiving zinc supplements zinc or zinc containing drugs were excluded. Twenty healthy hospital employees were studied as controls.

Clinical and laboratory investigations including liver function tests, prothrombin time and serum zinc levels were done. Sera were stored at 20°C and analyzed by atomic absorption spectrometry (Varian Techtron AA20) at a wavelength of 213.9 nm.

Fulminant and subacute hepatic failure were diagnosed based on criteria defined by Sherlock and Tandon respectively.

Statistical analysis was done using the Z test with significance accepted at a value greater than 1.96 (p<0.05).

Results

The mean duration of hepatic encephalopathy was 1.8 ±1.4 days. Thirty patients (18 women, 12 men; aged 39.8 ±16.0 yr) had fulminant hepatic failure (FHF) whereas, five had subacute hepatic failure with encephalopathy and twenty (2 women, 23 men, aged 36.8 ±14.4 yr) had chronic liver disease with encephalopathy. Grade I to III encephalopathy was present in 27 patients and grade IV or V encephalopathy in 28.

Serum zinc levels

Mean serum zinc levels were significantly (p<0.001) lower (71.9±15.8 µg/dL) in patients as compared to healthy controls (112.7±18.2 µg/dL). Zinc levels did not vary with age or sex or with grade and duration of encephalopathy.
Table 1: Laboratory investigations in the patient group

<table>
<thead>
<tr>
<th></th>
<th>Acute (n=30)</th>
<th>Subacute or chronic (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>19.5 ± 11.5</td>
<td>14.7 ± 7.4</td>
</tr>
<tr>
<td>Aspartate aminotransferase (IU)</td>
<td>962 ± 96</td>
<td>185 ± 170.5</td>
</tr>
<tr>
<td>Alanine aminotransferase (IU)</td>
<td>1448 ± 1320</td>
<td>140 ± 255.7</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU)</td>
<td>348 ± 189</td>
<td>272 ± 283.1</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.3 ± 0.8</td>
<td>2.62 ± 0.48</td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>39.2 ± 23.7</td>
<td>27.2 ± 10.0</td>
</tr>
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</table>

There was no significant difference in the serum zinc levels between patients with FHF (70.5 ± 14.7 μg/dL) and those with chronic liver disease (73.7 ± 5.4 μg/dL). Twenty alcoholic patients had serum zinc values similar to these in 35 non-alcoholics. Zinc levels were however significantly lower in patients with serum bilirubin greater than 23 mg/dL than in those with bilirubin < 23 mg/dL (64.7 ± 11.1 μg/dL vs. 74.4 ± 16.2 μg/dL) and in those with prothrombin time 12 seconds proposed beyond controls then in those with prothrombin time < 12 second beyond control (67.6 ± 12.1 μg/dL vs. 81.4 ± 16.8 μg/dL). Serum zinc levels did not correlate with liver span, presence of ascites, serum transaminases, serum alkaline phosphatase or serum albumin levels.

Seventeen of the 55 patients recovered, 3 died and seven left the hospital against medical advice. There was no correlation between serum zinc levels and mortality. However, in the 17 survivors, the mean serum zinc levels 24 h after complete clinical recovery were 64.6 ± 14.8 μg/dL compared to 74.1 ± 15.1 μg/dL during encephalopathy (p = ns).

Discussion

The mean serum zinc level in our control group (112.7 μg/dL) was within the normal range reported (76-222 μg/dL). The mean serum zinc in the patient group was significantly lower. These results are consistent with those of previous studies.4,6,9

There could be several reasons for low serum zinc levels in patients with cirrhosis. Levels of amino acids like cysteine and histidine increase by up to 20% during hepatic encephalopathy, leading to a shift of zinc from albumin and alpha-2 macroglubulin to non-protein ligands which get filtered across the glomerulus. This may lead to hyperzincuria and therefore decreased serum zinc. The renal clearance of zinc is up to three times greater in cirrhosis.5 A reduced hepatic extraction of zinc due to portal-systemic shunting in cirrhosis8 may lead to increased renal losses of zinc.9 Our patients with FHF and normal serum albumin also had low serum zinc levels. Mechanisms postulated for this include a shift of zinc during acute stress from plasma to liver via an mediator released from activated phagocytes. This mediator also stimulates the liver to produce a large number of acute phase reactant proteins which require zinc as a co-factor in their synthesis.11

Rise in serum bilirubin above 23 mg/dL carries a bad prognosis in patients with FHF.12 Our study as well as the previous studies13,14 have shown that serum zinc concentration varies inversely with serum bilirubin levels. Prolonged prothrombin time was associated with significantly lower serum zinc levels in our study; this is consistent with the finding reported by Weissemann et al.15

Though Singh et al.6 showed that serum zinc levels returned to normal four weeks after recovery, levels immediately after recovering from encephalopathy have not been studied. We observed that serum zinc levels did not return to normal immediately after recovery from encephalopathy in the 17 survivors. We believe that this may be due to the negligible amount of zinc in the standard hepatic coma feeds and increased excretion of zinc through bile and sweat in acute stress.11

References


