Correlation between albuminemia, natremia and survival rates in patients with hepatorenal syndrome

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Abstract
A two years prospective study was developed, based on the monitoring of 84 patients with cirrhosis and elevated serum creatinine; 33 patients met the diagnostic criteria for the hepatorenal syndrome. In these 33 patients, survival rate has been studied in correlation with hepatorenal syndrome types, serum albumin and natremia.

Keywords: hepatorenal syndrome, survival rate, albuminemia, natremia.

Introduction
Hepatorenal syndrome (HRS) is diagnosed by excluding other causes of renal impairment in patients with advanced liver disease and renal failure. It occurs in patients with hepatic failure, acute and chronic liver disease, and portal hypertension [1, 2]. Hepatorenal syndrome represents a functional and reversible renal failure [3]. Its diagnosis depends mainly on the serum creatinine level. Although its level is not a conclusive marker of the renal function in patients with cirrhosis, there are no other non-invasive markers, validated for monitoring the renal function in these patients [4, 5].

There are two forms of HRS: type I (acute), marked by a rapid progression of renal failure, and type II (chronic), characterized by a slowly progressive course and an insidious onset. In HRS type I we have an increased value of serum creatinine, up to at least 2.5 mg/dL within two weeks, often after a precipitating event such as infection. In HRS type II, we have a serum creatinine of at least 1.5 mg/dL and refractory ascites [6, 7].

Untreated hepatorenal syndrome type I has a mortality of 80% in two weeks; only 10% of the patients survive more than three months. By contrast, patients with hepatorenal syndrome type II have a better average survival rate, about six months [8].

Results
From the 33 patients with hepatorenal syndrome, 14 had serum creatinine over 4.5 mg/dL and 19 presented values below 4.5 mg/dL. The 19 patients required hemodiafiltration (HDF), as they presented the following characteristics:

- values of serum creatinine over 4.5 mg/dL, and/or
- severe metabolic acidosis – alkaline reserve below 18 mEq/L, and/or
- hyperkalemia: serum K⁺ over 6.5 mEq/L, and/or
- persistent oligoanuria: diuresis less than 400 mL/24 hours extended over 48 hours.

The group of patients with hepatorenal syndrome was also divided according to the serum sodium values, as follows:
Monitoring the evolution of all patients with hepatorenal syndrome, we could determine the survival patterns in the two groups:

- patients with HRS that required HDF presented survival rates between 5 and 14 days;
- patients who had initial creatinine value <4.5 mg/dL, monitored ambulatory, survived between 87 and 279 days.

Thus, we can divide the 33 patients with hepatorenal syndrome in hepatorenal syndrome type I (14 patients) and type II (19 patients).

Among those with creatinine values below 4.5 mg/dL, two patients received liver transplantation in Fundeni Clinical Hospital. Liver transplantation is the ideal treatment in patients with hepatorenal syndrome; death occurs in the majority of the patients, before the transplantation, due to the long waiting lists. Alternative therapies are required to increase the survival rate in these patients, until the liver transplantation can be performed [10, 11]. In a recent study it was shown that survival was better in patients who responded to other type of therapy and depends on age ($p=0.017$), bilirubin ($p=0.012$), and creatinine level [12]. Their post-transplant evolution exceeded two months, they could no longer be monitored within our Nephrology Department, and so their survival rate remained unknown.

Statistically analyzing the data, we compared the survival rate in HRS patients depending on serum sodium values (Figures 1–4, Tables 1–3).

It is shown that patients with HRS with the lowest survival rate (less than 10 days) are the ones having minimal serum sodium value (below 120 mEq/L).

Patients with survival rate between 10 and 14 days are the ones with serum sodium value between 120–125 mEq/L.

In the group of 19 patients (HRS type II), long-term survival (more than six months) was noticed in those with measured Na value between 125–130 mEq/L, and below an average survival rate of 6 months, in those with sodium value between 120–124 mEq/L. Two patients were excluded out of the 33 – those who received liver transplant and whose survival rate is unknown (Figure 5, Table 4).
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Among the features that have been analyzed within the overall group of patients and subgroup with HRS, it has been concluded that only a few can be used as guidance prognostic factors of evolution in HRS. In these patients, using statistical Z-test, it has been established that the liver morphological type is, with few exceptions, hypotrophic ($p > 0.90$), have prothrombin index below 75% ($p > 0.90$), serum bilirubin without a distribution pattern, viral etiology and Child C type affiliation being almost a rule [13]. These parameters were not able to provide prognostic elements either due to the reduced number of cases that differ from the majority, or because of random distribution.

In this case, the only variable that could be fitted in groups of values with statistical significance was the serum albumin (Figure 6).

![Figure 5 – Survival rate depending of serum sodium values in type II HRS.](image)

Survival in patients with type II HRS depends on the values of albumin and sodium (the higher the albumin and sodium are, the higher the survival rate is), while in patients with type I HRS, survival rate depends only on the sodium value (Table 5).

Table 4 – Na+ values correlated with survival rates in patients with type II HRS

<table>
<thead>
<tr>
<th>Survival [days]</th>
<th>87 98 122 123 135 135 139 169 175 176</th>
<th>Average rate</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+ value [mEq/L]</td>
<td>123 122 123 123 122 124 122 124 124 124</td>
<td>136 31</td>
<td></td>
</tr>
<tr>
<td>Survival [days]</td>
<td>182 189 transplant 202 254 256 279 230</td>
<td>227 37</td>
<td></td>
</tr>
<tr>
<td>Na+ value [mEq/L]</td>
<td>125 126 127 127 128 127 129 126 127 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5 – Na+ and albumin values correlated with survival rates in type II HRS patients

<table>
<thead>
<tr>
<th>Survival [days]</th>
<th>87 123 139 122 135 98 189 176 254 175 182 230</th>
<th>Average rate: 175</th>
<th>SD: 56</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+ value [mEq/L]</td>
<td>123 122 123 122 123 122 122 126 123 128 124 125 126</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin [g/dL]</td>
<td>2.6 2.8 169 2.6 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival [days]</td>
<td>153 202 279 169 256</td>
<td>Average rate: 124</td>
<td>SD: 2</td>
</tr>
<tr>
<td>Na+ value [mEq/L]</td>
<td>124 125 129 124 127</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin [g/dL]</td>
<td>2.6 2.8 2.6</td>
<td>Average rate: 2.7</td>
<td>SD: 0.2</td>
</tr>
</tbody>
</table>

Discussion

Following patients with HRS, we observed differences in the biological constants values, in order to determine which of them can be prognostic factors.

Fourteen of the patients had creatinine values over 4.5 mg%, acidosis, persistent oliguria with hyperkalemia and required HDF.

HRS patients that required HDF had survival rates average 9.57 days.

Patients that had initial creatinine values <4.5 mg/dL, being under periodical ambulatory supervision, survived average 174.64 days. Differences in the survival rate can be noticed. The type of therapy, resulted from the severity of the renal disease, is a prognostic factor in the evolution of HRS.

Serum albumin values influenced the survival rates in patients with type II HRS; patients with higher albumin values have longer survival rates.

Blood sodium levels influence the rate of survival in both patients with type I HRS, and those with type II HRS. The average length of survival decreases following sodium values.

![Figure 6 – Survival rate depending on the values of albumin in patients with type II HRS.](image)

Survival in patients with type II HRS is long enough to allow liver transplantation. Clinical applicability of liver transplantation in patients with type I HRS is limited by their short survival and long waiting lists [14, 15].
Conclusions

In conclusion, survival in patients with type II HRS was influenced both by albumin values and serum sodium ones (the higher the albumin and serum sodium are, the higher the survival rate is), while in patients with type I HRS the rate of survival depends only on the sodium value. This may have as cause the “liver out” syndrome that can occur in type I HRS patients (very low serum albumin values, the prothrombin index, etc.).

References


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