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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 diagnosticated 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].

Patients and Methods

A two years prospective study developed in the Nephrology Department of "St. John" Clinical Emergency Hospital, Bucharest, between January 2008 and January 2010, focused on the monitoring of 84 patients with cirrhosis and elevated serum creatinine. The group of 84 patients underwent clinical, biological and non-invasive laboratory follow-up during the study. We split the initial study group into groups of patients according to the values of the following parameters: ultrasound structure of the liver, serum albumin values, prothrombin index, bilirubin and the etiology of cirrhosis.

Out of the 84 patients, only 33 met the diagnostic criteria established by the *International Ascites Club* (IAC) in 1996 for the hepatorenal syndrome:

- diuresis less than 500 mL/day;
- serum creatinine over 1.5 mg% at 48 hours after therapy test initiation: fluid loading and diuretic removal;
- the absence of shock;
- lack of nephrotoxic administration;
- absence of gastrointestinal losses [9].

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 hemo-diafiltration (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:

- serum Na^+ 130–125 mEq/L: nine patients;
- serum Na^+ 124–120 mEq/L: 17 patients;
- serum Na^+ <120 mEq/L: seven patients.

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).

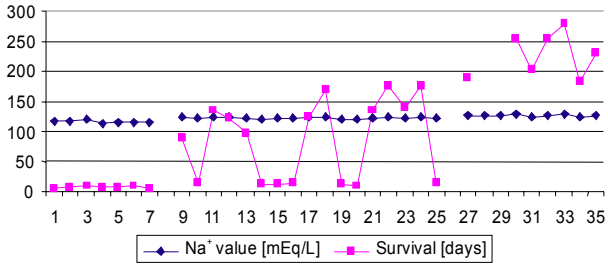

Figure 1 – ***Survival rate depending on serum sodium values.***

Table 1 – ***Serum sodium values <120 mEq/L***

								Average rate	SD
Na^+ value [mEq/L]	117	115	119	113	115	116	115	*116*	*2*
Survival [days]	5	7	10	6	7	9	4	*7*	*2*

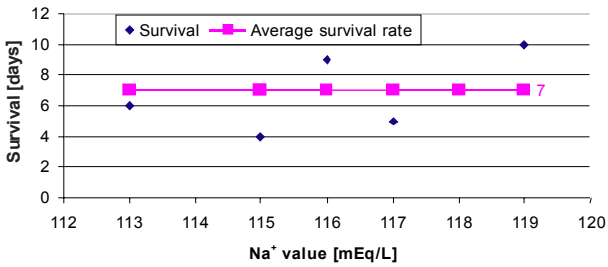

Figure 2 – ***Survival rate depending on serum sodium values (Na^+<120 mEq/L).***

Table 2 – ***Serum sodium values between 120 and 124 mEq/L***

Na^+ value [mEq/l]	123	121	124	123	122	120	121	122	123
Survival [days]	87	14	135	122	98	12	12	14	123
Na^+ value [mEq/L]	124	120	120	122	123	122	124	121	–
Survival [days]	169	11	10	135	176	139	175	13	–

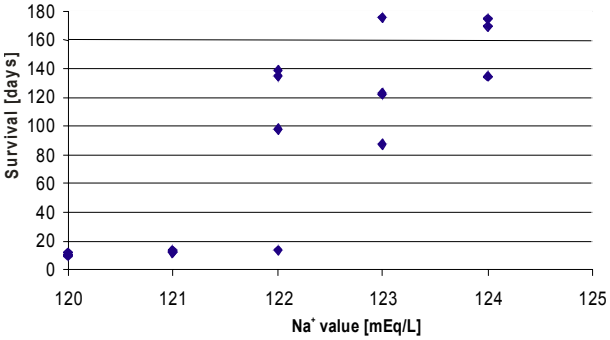

Figure 3 – ***Survival rate depending on serum sodium values (Na^+ between 120 and 124 mEq/L).***

Table 3 – ***Serum sodium value between 125 and 130 mEq/L***

									Average rate	SD
Na^+ value [mEq/L]	126	126	127	128	125	127	129	125	126	*127*	*1*
Survival [days]	189	transplant	254	202	256	279	182	230		*227*	*37*

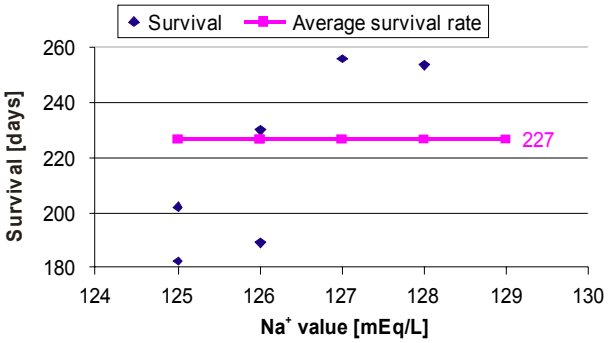

Figure 4 – ***Survival rate depending on serum sodium values (Na^+ between 125 and 130 mEq/L).***

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).

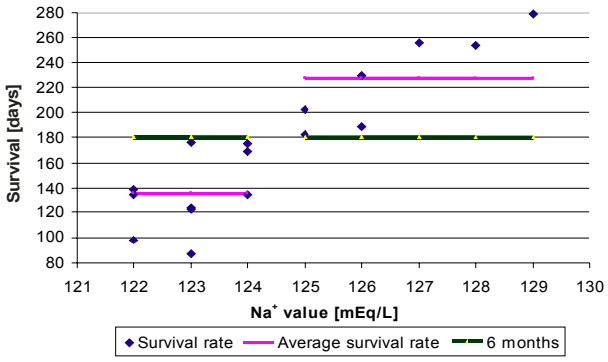

Figure 5 – *Survival rate depending of serum sodium values in type II HRS.*

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).

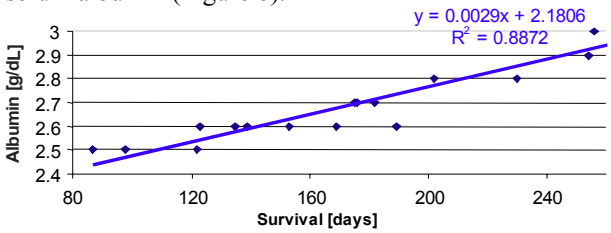

Figure 6 – *Survival rate depending on the values of albumin in patients with type II HRS.*

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*

											Average rate	SD
Survival [days]	*87*	98	122	123	135	135	139	169	175	176	*136*	*31*
Na^+ value [mEq/L]	*123*	122	123	123	122	124	122	124	124	123	*123*	*1*
Survival [days]	182	189	transplant			202	254	256	279	230	*227*	*37*
Na^+ value [mEq/L]	125	126	126		127	125	128	127	129	126	*127*	*2*

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

Survival [days]	*87*	123	139	122	135	98	189	176	254	175	182	230
Na^+ value [mEq/L]	*123*	123	122	123	122	122	126	123	128	124	125	126
Albumin [g/dL]	*2.5*	2.6	2.6	2.5	2.6	2.5	2.6	2.7	2.9	2.7	2.7	2.8
Survival [days]	153	202	279	169	256	*Average rate:*		*175*			*SD:*	*56*
Na^+ value [mEq/L]	124	125	129	124	127	*Average rate:*		*124*			*SD:*	*2*
Albumin [g/dL]	2.6	2.8	169	2.6	3	*Average rate:*		*2.7*			*SD:*	*0.2*

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 rates 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.

Among the features that we have studied in the group of patients, we observed that only a small part turned out to have a significant influence on the evolution of HRS, according to the statistical analysis:

- in the subgroup of patients with type I HRS, the lowest survival rate (less than 10 days) was registered among the subpopulation with the lowest values of serum sodium (below 120 mEq/L); patients with serum sodium values between 120–125 mEq/L had a survival rate between 10 and 14 days;
- in the subgroup with type II HRS, the longest survival rate (more than six months) was noticed in cases where serum sodium values reached 125–130 mEq/L, while when serum sodium values were between 120–124 mEq/L, the average survival rate was less than six months; in patients with type II HRS, higher values of albumin were correlated with longer survival periods: R^2=0.846.

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.).

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