WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 17, 779-790. Research Article ISSN 2277– 7105

STUDY OF CORRELATION OF UREA, CREATININE, SODIUM, POTASSIUM AND CHLORIDE CONCENTRATION BETWEEN ASCITIC FLUID AND VENOUS BLOOD IN ALCOHOLIC LIVER DISEASE

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Article Received on
07 August 2018,

Revised on 27 August 2018,
Accepted on 17 Sept. 2018

DOI: 10.20959/wjpr201817-13130

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ABSTRACT

Treatment of ascitic cirrhosis requires monitoring of blood biochemistry. Regular blood sampling can become difficult in these patients due to their limited venous access. A direct measure of ascites could simplify the medical procedure. This strategy depends on an excellent correlation between venous blood and ascitic fluid levels of the various biochemical parameters monitored. Hence we have studied the correlation of urea, creatinine and electrolytes between ascitic fluid and venous blood in cirrhosis, both before diuretics and after initiating diuretics. The study was conducted in over a period of 24 months in Goa Medical College and Hospital. Diagnosis and classification of cirrhosis was made based on Childpugh Classification and signs and symptoms like swelling of abdomen, asterixis, gynaecomastia, spider angioma, palmar, erythema, duputryen contracture, pedal edema, jaundice, parotid swelling, inversion of sleep rhythm, past history of melena, past history of hematemesis, anorexia, weakness and pallor. Two hundred concomitant ascitic fluid and blood samples were obtained from 100 patients, at first visit (before diuretic therapy) and after initiating diuretic therapy. In ascetic fluid and blood of cirrhotic patients at first visit the results were respectively 28.41±6.943 and

29.43±6.958 for Urea (r=0.984, p<0.0001), 0.919±0.2145 and 1.022±0.2205 for creatinine (r=0.829, p<0.0001), 133.87 ± 4.136 and 131.88±4.083 for Na(r=0.968, p<0.0001), 3.994±0.5158 and 4.061±0.5162 for K(r=0.961, p<0.0001), 105.59±5.932 and 102.98±6.055for Cl (0.980, p<0.0001). After initiating diuretic therapy, the results in ascitic fluid and blood were, respectively 28±6.515 and 28.66±6.643 for urea (r=0.993, p<0.0001), 0.941±0.1826 and 1.023±0.1791 for creatinine (r=0.845, p<0.0001), 133.79±3.301 and 131.87±3.199 for Na (r=0.953, p<0.0001), 4.064±0.4679 and 4.128±0.4513 for K (r=0.965, p<0.0001) and 106.03±5.355 and 105.52±5.194 for Cl (r=0.965, p<0.0001) thereby concluding the strong correlation for Na, K, Cl, Urea, and Creatinine between ascitic fluid and venous blood in cirrhotic patients and also a strong correlation for Na, K, Cl, Urea, and Creatinine are strong between ascites and venous blood in cirrhotic patients both before diuretics and after initiating diuretics.

KEYWORDS: Cirrhosis, Acites, Diuretic, Paracentesis.

INTRODUCTION

The treatment of ascites in cirrhotic patients by sodium restriction, diuretics and/or paracentesis requires monitoring of serum sodium, potassium and renal function parameters to detect adverse effects of drug therapy. Regular blood sampling can become difficult in these patients due to their limited venous access. These tests could be performed directly in ascitic fluid obtained during routine paracentesis in, for example, patients without venous access or when biochemical measurements such as liver tests or coagulation tests are not required, or when venous access is limited. This strategy depends on an excellent correlation between venous blood and ascitic fluid levels of the various biochemical parameters monitored. This correlation has not been clearly established and may depend on many factors such as liver function or complications of cirrhosis, composition of ascites, renal function, sodium intake and perhaps diuretics. Hence we have studied the correlation of urea, creatinine and electrolytes between ascitic fluid and venous blood in cirrhosis, both before diuretics and after initiating diuretics. The objective of this study was to prospectively study the correlation between venous blood and ascitic fluid sodium (Na), potassium (K), chloride (Cl), urea (U) and creatinine (Creat.) concentrations in cirrhotic patients with ascites in alcoholic liver disease, to monitor diuretic therapy based on ascitic fluid electrolytes and usage of ascitic fluid urea, creatinine and electrolytes in patients having poor venous access and abnormal coagulation profile.

MATERIALS AND METHODS

Study of correlation of urea, creatinine and electrolytes between ascitic fluid and venous blood in cirrhosis due to alcohol was carried out in the department of Medicine, Goa Medical College Hospital.

METHODOLOGY

1. Patients

A total of 100 cirrhotic patients with ascites in whom etiological diagnosis being alcoholic liver disease, admitted in the department of Medicine, Goa Medical College were studied prospectively. Protocol was approved by hospital's ethical committee and an informed consent was obtained from all patients. On entry, a detailed history and clinical examination were conducted. The 100 patients who satisfied the set criteria were included.

Inclusion Criteria

a. History of alcohol consumption of atleast 160gm/day for atleast 10 years.
b. Uncomplicated cirrhosis

Exclusion Criteria

a. Complicated cirrhosis
b. Patients with hepatitis B and hepatitis C positivity
c. Patients with gross electrolyte abnormality at the time of admission
d. Patients with chronic kidney disease, Chronic diarrhea, Congestive cardiac failure and Diabetes mellitus
e. Patients on diuretics and steroids at the tim e of admission
f. Family history of liver disease
g. Cirrhosis due to NAFLD
h. Family history of neuropsychiatric manifestation.

Cirrhosis due to alcohol was diagnosed on basis of clinical, laboratory and ultrasonography evidence.

Cirrhosis was classified according to Child-Pugh classification.

Ascites was classified as

Grade 1: detected by ultrasonography

Grade 2: moderate symmetrical distension of abdomen

Grade 3: marked abdominal distension

Blood samples were collected from anticubital veins under strict aseptic precautions.

Ascitic fluid samples were collected by abdominal paracentesis under strict aseptic precautions simultaneously.

Urea, creatinine and electrolytes were measured in all samples using biochemical autoanalyzer.

All patients were advised

1. Salt restricted diet (less than 5gm per day)
2. Spirinolactone 100 mg od
3. Furosemide 40 mg od
4. Lactulose 30 cc bd
5. Propranolol 10 mg tds
6. Isosorbide mononitrate 20 bd
7. Thiamine 75 mg od

All patients were asked to follow up after 7 days.

At follow up, blood samples were collected from anticubital veins under strict aseptic precautions and ascitic fluid samples were collected by abdominal paracentesis under strict aseptic precautions simultaneously.

Urea, creatinine and electrolytes were measured in all samples using biochemical autoanalyzer.

Statistical analysis was performed.

Concentrations of the various parameters were expressed as mean±standard deviation (SD) and were compared using a paired student t-test.

The correlation between values in ascites and venous blood was tested by calculating the correlation coefficient (r).

A difference was considered to be statistically significant for p value below 0.05.

RESULTS

Two hundred concomitant ascitic fluid and blood samples were obtained from 100 patients. The results of the diagnostic ascitic fluid aspiration and the venous blood sample in all the hundred selected patients are being interpreted here.

Table 1: Age Wise Distribution.

Age(years)	Total
21-30	5
31-40	26
41-50	35
51-60	26
61-70	7
71-80	1

Table 2: Duration of Alcoholism.

Number of Years	Number of Patients
10-15	49
16-20	25
21-25	16
26-30	7
31-35	3

Table 3: Childpugh Classification of Cirhosis.

Childpugh Classification	Number of Patients
B	44
C	56

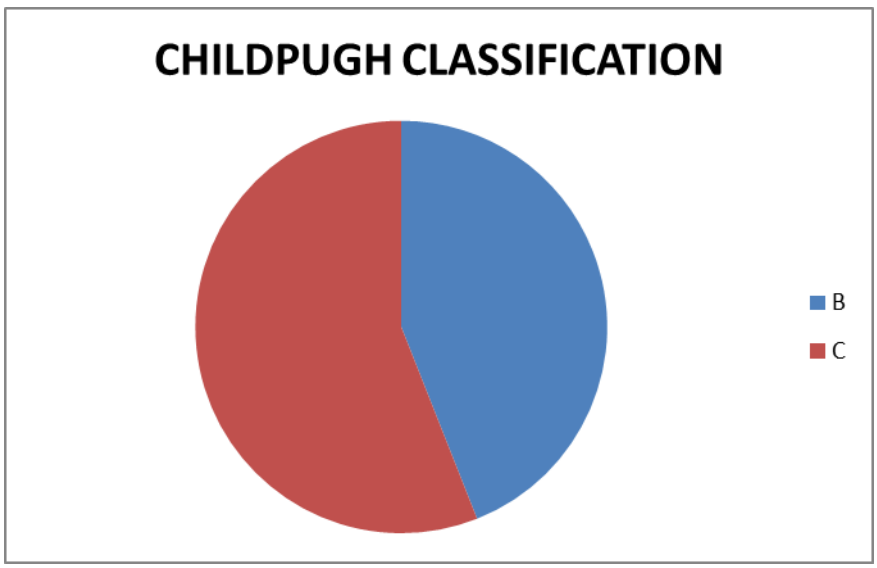


Figure 1.

Table 4: Grade of Ascites.

Grade of Ascites	Total
2	49
3	51

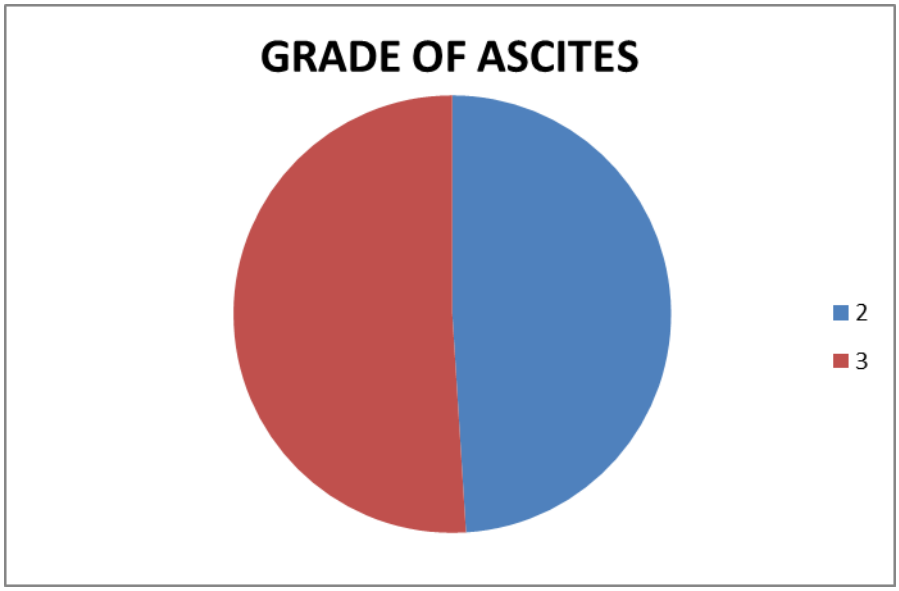
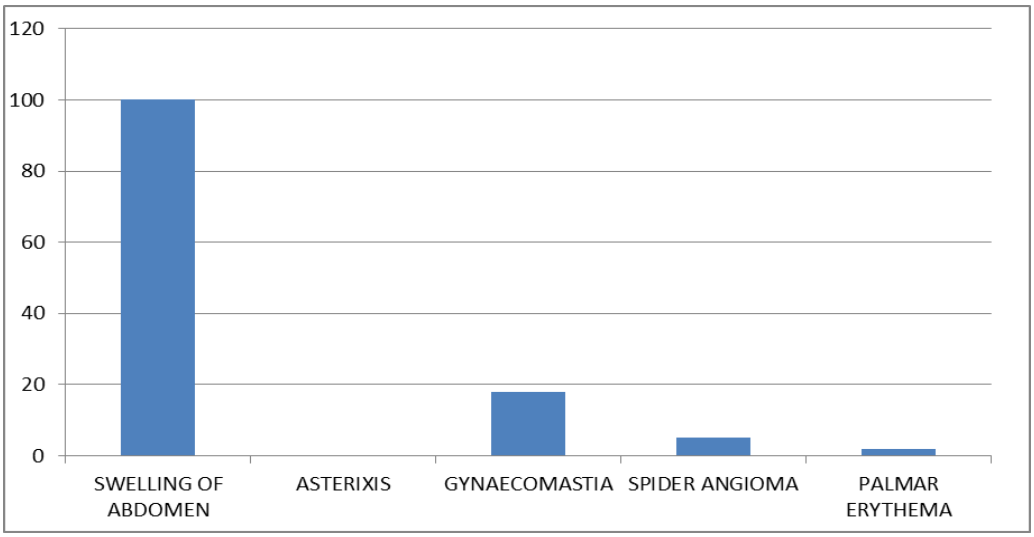


Figure 2.

Table 5: Signs and Symptoms.

Clinical Parameter	Number of Patients	Percentage
SWELLING OF ABDOMEN	100	100
ASTERIXIS	0	0
GYNAECOMASTIA	18	18
SPIDER ANGIOMA	5	5
PALMAR ERYTHEMA	2	2
DUPUTRYEN CONTRACTURE	0	0
PEDAL EDEMA	100	100
JAUNDICE	67	67
PAROTID SWELLING	8	8
INVERSION OF SLEEP RYTHM	2	2
PAST HISTORY OF MELENA	4	4
PAST HISTORY OF HEMATEMESIS	2	2
ANOREXIA & WEAKNESS	100	100
PALLOR	28	28



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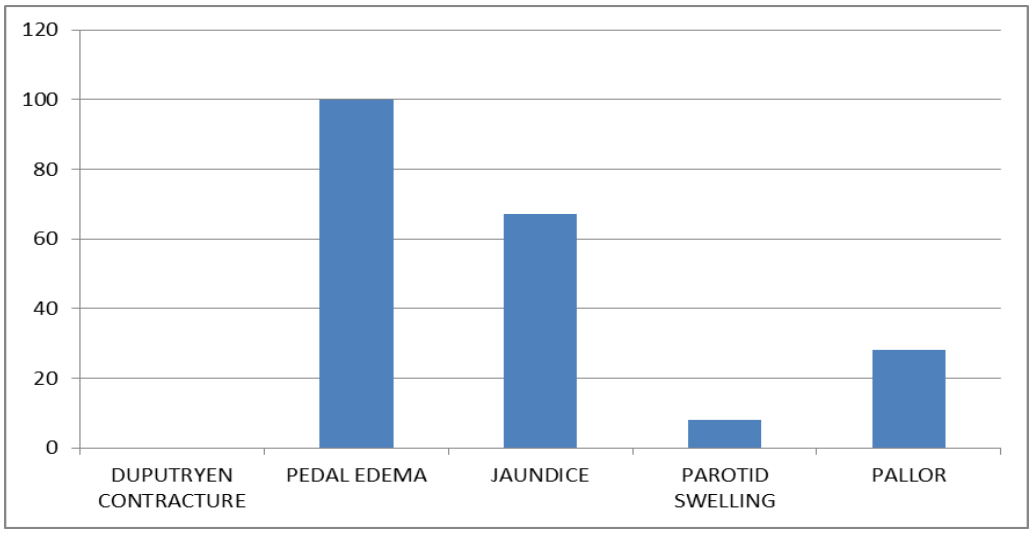

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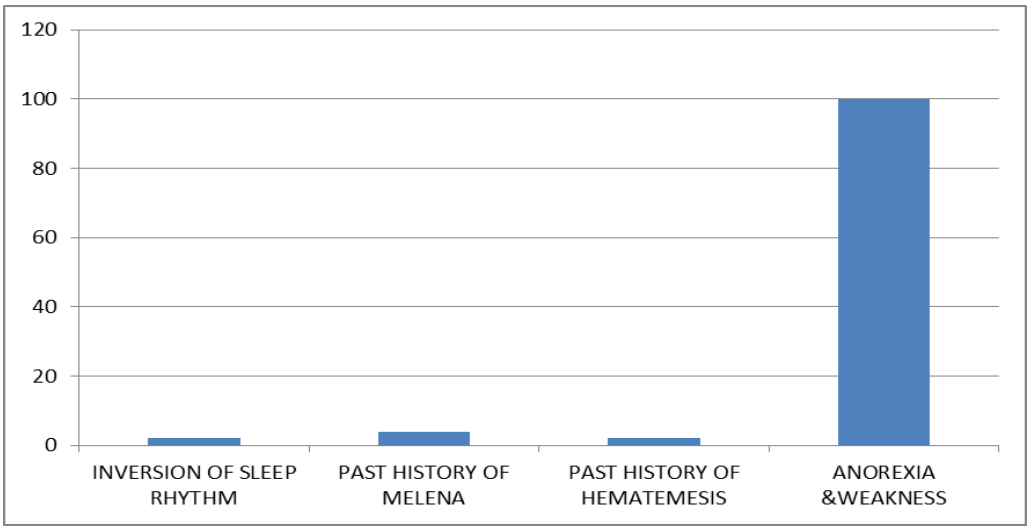

Figure 5.

Table 6: Correlation of ascites and blood (first visit).

	Ascites	Blood	Student p	r	p
Urea	28.41±6.943	29.43±6.958	<0.0001	0.984	<0.0001
Creatinine	0.919±0.2145	1.022±0.2205	<0.0001	0.829	<0.0001
Na	133.87±4.136	131.88±4.083	<0.0001	0.968	<0.0001
K	3.994±0.5158	4.061±0.5162	<0.0001	0.961	<0.0001
Cl	105.59±5.932	102.98±6.055	<0.0001	0.980	<0.0001

Table 7: Correlation of ascites and blood (after diuretic therapy).

	Ascites	Blood	Student p	r	p
Urea	28±6.515	28.66±6.643	<0.0001	0.993	<0.0001
Creatinine	0.941±0.1826	1.023±0.1791	<0.0001	0.845	<0.0001
Na	133.79±3.301	131.87±3.199	<0.0001	0.953	<0.0001
K	4.064±0.4679	4.128±0.4513	<0.0001	0.965	<0.0001
Cl	106.03±5.355	105.52±5.194	<0.0001	0.965	<0.0001

DISCUSSION

In ascites and blood the results were, respectively 28.41±6.943 and 29.43±6.958 for Urea (r=0.984, p<0.0001), 0.919±0.2145 and 1.022±0.2205 for creatinine (r=0.829, p<0.0001), 133.87±4.136 and 131.88±4.083 for Na(r=0.968, p<0.0001), 3.994±0.5158 and 4.061±0.5162 for K(r=0.961, p<0.0001), 105.59±5.932 and 102.98±6.055for Cl (0.980, , p<0.0001).

Following results were obtained after initiating diuretic therapy.

In ascites and blood the results were, respectively 28±6.515 and 28.66±6.643 for urea(r=0.993, p<0.0001), 0.941±0.1826 and 1.023±0.1791 for creatinine(r=0.845, p<0.0001), 133.79±3.301 and 131.87±3.199 for Na(r=0.953, p<0.0001), 4.064±0.4679 and 4.128±0.4513 for K(r=0.965, p<0.0001) and 106.03±5.355 and 105.52±5.194 for Cl(r=0.965, p<0.0001).

Correlations for Na, K, Cl, U, and Creat are strong between ascites and venous blood in cirrhotic patients both before diuretics and after initiating diuretics.

In a study conducted by Eric Nguyen-Khac et al 2001, Ascitic fluid and venous blood samples were collected simultaneously from 70 cirrhotic patients. Na, K, Cl, U, and Creat were measured in all samples using a biochemical auto-analyzer.

Results are expressed as the mean and SD of 200 concomitant samples of ascitic fluid and venous blood (mmol/L for Na,K, and Cl; g/L for U; mg/L for Creat).

In ascites and blood the results were, respectively: 133.1±6.6 and 131.8±6.3 for Na ($p<0.0001$, $r=0.95$), 4.1±0.8 and 4.3±0.9 for K ($p<0.0001$, $r=0.90$), 107.2±7.6 and 101±7 for Cl ($p<0.0001$, $r=0.93$), 0.54±0.52 and 0.53±0.5 for U ($p<0.0001$, $r=0.99$), and 9.8±7.5 and 11±7 for Creat ($p<0.0001$, $r=0.99$).

In 1986, Ballarin et al. reported the presence of a high correlation for Na, K, pH, and phosphorus between ascites and blood in a series of 19 cirrhotic patients. No correlation was observed for transaminases and LDH. Although this small series did not describe the clinical characteristics of cirrhosis and diuretic therapy, the authors concluded that an assay of these electrolytes in ascites could be clinically useful. The correlations for Na ($r=0.79$) and K ($r=0.83$) were lower than those observed in our study ($r=0.968$) and 0.961, respectively), possibly because of the smaller sample size.

Mukherjee et al., in 1988, also studied the correlation of Na, K, and Cl levels in portal and venous blood (taken from portosystemic shunts at the umbilicus) compared to ascites in 20 cirrhotic patients reported a correlation coefficient of 0.74 for Na, but a poor correlation for K and Cl.

Table 8: Correlation coefficient comparison.

	Urea	Creatinine	Na	K	Cl
Present study	0.984	0.829	0.968	0.961	0.98
Present study (after diuretic)	0.993	0.845	0.953	0.965	0.965
Eric Nguyen-Khac et al	0.99	0.99	0.95	0.90	0.93
Ballarin et al			0.79	0.83	
Mukherjee et al			0.74	Poor correlation	Poor correlation

In a study conducted by Kelton JG et al 50 peritoneal fluid samples were taken before 106 peritoneal dialysis sessions in five patients and compared to venous blood levels. The authors reported correlation coefficients of 0.82, 0.95, 0.98, and 0.96 for Na, K, U, and Creat, respectively.

Study by Selgas Gutierrez R et al 53 peritoneal samples were taken from 16 patients and compared to venous blood levels.

Correlation coefficients were 0.34, 0.64, 0.57, and 0.74 for Na, K, Cl, and Creat, respectively, and a higher correlation coefficient of 0.92 was observed for U.

Manahan et al study demonstrated a correlation for U and Creat in 22 women undergoing hysterectomy, in whom peritoneal fluid samples were taken on day 3 and compared with serum levels. In this study, the results from peritoneal fluid were useful in distinguishing postoperative ascites from traumatic urinary Fistula.

The results obtained in cirrhotic patients cannot be compared to those obtained in non-cirrhotic patients due to the different pathophysiological mechanisms involved. In peritoneal dialysis, an extrinsic solution is introduced into the peritoneal cavity at each session.

The electrolyte balance is gradually achieved across the semi-permeable membrane of the peritoneum. Assays performed at various times on the dialysate could account for the different correlations reported in the various studies. In cirrhotic patients, portal hypertension and salt and fluid retention are responsible for the formation of ascites. After in vivo ligation of the superior venacava in the cat, venous hypertension is immediately transmitted to the hepatic sinusoids. Blood then leaves the sinusoid capillaries via pores, 100–500 nm in diameter.

Increased low molecular weights of these compounds probably facilitates their passage through the sinusoids. However, cirrhosis is accompanied by capillary transformation of the sinusoids. The pore diameter is decreased, which could account for the absence of correlation for large molecular weight molecules such as proteins.

CONCLUSIONS

Following conclusions were obtained:

1) Correlations for Na, K, Cl, U, and Creat are strong between ascites and venous blood in cirrhotic patients.

2) Correlations for Na, K, Cl, U, and Creat are strong between ascites and venous blood in cirrhotic patients both before diuretics and after initiating diuretics.

3) The results obtained in cirrhotic patients cannot be compared to those obtained in non-cirrhotic patients due to the different pathophysiological mechanisms involved.

4) Values of sodium and chloride were higher in ascites compared to blood. Study conducted by Eric Nguyen-Khac et al also obtained the similar results. Mukherjee et al also demonstrated similar results. Mehrotra MP et al showed similar findings.

The likely explanation for this finding is involvement of active secretory processes in the peritoneum for sodium and chloride.

Practical implications of direct assay of these biochemical parameters in ascites

Ascitic fluid parameters are commonly used for the diagnosis of certain complications of cirrhosis, such as spontaneous bacterial peritonitis, prediction of the risk of spontaneous bacterial peritonitis or its recurrence.

Monitoring of diuretic therapy requires regular monitoring of serum electrolytes and renal function in venous blood samples. The results of the study show that these tests can be performed directly in ascites during routine therapeutic paracentesis if taking a blood sample is difficult or impossible, especially in patients with known cirrhosis who have already undergone thorough assessment of their disease.

In this setting, blood tests become useless. This strategy also helps to preserve the patient's venous integrity.

Learning points

1) Electrolytes in ascitic cirrhosis (Na, K, U, and Creat) were very strongly correlated with serum concentration.

2) Correlations for Na, K, Cl, U, and Creat are strong between ascites and venous blood in cirrhotic patients both before diuretics and after initiating diuretics.

3) If taking a blood sample is difficult or impossible, especially in patients with known cirrhosis, electrolyte ascites could be used for diuretic monitoring.

4) Electrolyte assays can be performed routinely in the laboratory using an automatic serum analyzer.

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