Large Volume Paracentesis Associated with Intravenous Albumin Management of Patients With Cirrhosis and Ascites

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Özet: *ASİTLİ SİROZ HASTALARINDA İNTRAVENÖZ ALBUMİN EŞLİĞİNDE BÜYÜK VOLÜM PARASENTEZİN TEDAVİDEKİ ETKİNLİĞİ*

Günümüzde siroza bağlı asitin tedavisinde en çok kullanılan yöntem sodyumdan kısıtlı diyet ve diüretiklerdir. Fakat son yıllarda diyetle istenilen sonuçların alınamaması, diüretiklerle hepatik ensefalopati, böbrek yetmezliği ve elektrolit imbalansı gibi ağır komplikasyonların ortaya çıkması tedavide yeni arayışlara yönelinmesine neden olmuştur. Altermatiflerden biri; büyük volüm parasentezin yeniden gündeme gelmesidir.

Çalışmamızda intravenöz (i.v) human albüminle birlikte büyük volüm parasentezin etkinliği araştırılmıştır. 12 Child C grubunda olan siroz hastası çalışma grubuna alındı. Hastalara i.v 40.8 ± 3.9 gr (20–120) human albümin (Merieux human albümin % 20) eşliğinde 6.54 ± 1.3 lt. (4 – 12) parasentez yapıldı.

Hastalarda işlem sonrasında diastolik kan basıncı, kilo, serum globulini ve hematokritte düşme saptanırken ($p<0.05$), serum albümini ve ejeksiyon fraksiyonunda yükselmeler gözlendi ($p<0.05$). Diğer parametrelerde anlamlı değişiklikler saptanmadı. Hastaların daha sonraki izlemleri sırasında ilk ay sonunda anlamlı kilo artışları gözlenmedi.

Sonuç olarak i.v human albümin ile birlikte uygulanan büyük volüm parasentezin geç dönemde de etkili olan güvenli, kolay uygulanabilir ve hastanede kalma süresini kısaltan bir tedavi yöntemi olduğu düşünülmektedir.

Anahtar kelimeler: siroz, asit, albümin, parasentez.

Summary: *Large-volume paracentesis is an effective and safe therapy of ascites in patients with cirrhosis provided albumin is infused intravenously (i. v.). Twelve patients were treated with paracentesis 6.54 ± 1.3 lt and i. v. albumin infusion (40 ± 3.9 gr) after tape. Hemodynamic, renal and hepatic functions evaluation were performed before and after large-volume parasentesis associated with i. v. albumin. The volume of ascites removed was 6.54 ± 1.31 lt (range 4-12) per patient. The mean loss of body weight was 7.21 ± 0.35 kg. Periferal edema decreased markedly or resolved completely after treatment in all of the 8 patients exhibiting it. There were no local complications related to the procedure in 11 patients. One patient ascitic fluid leaked from the puncture hole for several hours after the paracentesis. After albumin administration decreased in the hematocrite from 30 ± 1.08 to 28 ± 1.68 ($p<0.004$) serum albumin increased from 2.59 ± 0.19 to 2.85 ± 0.10 gr ($p<0.02$) and cardiac ejection fraction from 61 ± 3.67 to 66 ± 2.30 % ($p< 0.007$). No significant changes were found in mean arterial pressure, heart rate, protrombin time, cardiac output and cardiac index at the end of the study. Body weight dropped significantly from 72.33 ± 5.09 to 65.12 ± 4.74 kg ($p<0.006$). Serum sodium showed in two patients developed hyponatremia that required no treatment. After albumin administration decreased the mean diastolic blood pressure from 65.83 ± 4.34 to 57.5 ± 1.79 mmHg ($p<0.001$). Renal and hepatic functions were measured after the administration of albumin and no significant changes were observed.*

These results indicate that total paracentesis associated with i. v. albumin can be safely performed in cirrhotic patients with tense ascites and suggest that these patients could be treated in a single-day hospitalization regime.

Key words: Cirrhosis, ascites, albumin, paracentesis.

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Tense ascites is a common clinical problem in patients with chronic liver disease and portal hypertension. It can be uncomfortable, cause respiratory distress, promote the formation and rupture of umblical hernias and have negative effects on cardiovascular function (1-4).

At present, the most widely used therapy for ascites in patients with cirrhosis is low sodium diet and diuretics. This treatment, however, is not entirely satisfactory. Because profound diuresis in these patients often associated with renal impairment, electrolyte disturbances, and hepatic encephalopathy, it is generally recommended that diuretic dosage should be adjusted to produce a loss of body weight of about 500 g/day (5-9). This means that the mobilization of a tense ascites requires a prolonged hospital stay in most cases. In addition, despite long-term diuretic treatment, a high proportion of these patients have to be readmitted several times during the course of the disease because of reaccumulation of ascites. Finnally 20% of cirrhotics with ascites admitted to a general hospital do not respond to diuretics (10). It is not surprising, therefore, that alternative methods for the treatment of ascites are currently being investigated by several groups.

Paracentesis, the oldest form of therapy for ascites, is a rapid and effective treatment of this complication. This procedure was abondoned after the introduction of the modern diuretics because it was generally considered at that time that it could induce serious complications, such as bacterial peritonitis, severe hypovolemia, renal failure, hyponatremia, protein depletion, and hepatic encephalopathy (3,11-15).

Previous investigations have shown that repeated large-volume paracentesis (4-6 L/day) until complete mobilization of the intraabdominal fluid plus i. v. albumin (20-60 g/day) is a fast effective, and safe therapy of ascites in patients with cirrhosis (16-18), and that the i. v. administration of albumin is essential to prevent the impairment of systemic hemodynamics and renal function that frequently occur when repeated large-volume paracentesis is performed without intravascular volume expansion (19). The current study was undertaken to investigate whether tense ascites in cirrhosis can be mobilized in only one paracentesis session without adverse effects on systemic hemodynamics and renal function.

MATERIALS and METHODS

The study was made in 12 patients admitted for the treatment of ascites in the hospital of Ondokuz Mayıs University, School of Medicine, Samsun-Turkey between 1991-1992.

The criteria used to admit patients into the study were the following: a) cirrhosis with tense ascites (diagnosis of cirrhosis was based on liver histology and on clinical and laboratory data, b) no clinical, laboratory, or echographic data suggesting hepatocellular carcinoma; c) absence of hepatic encephalopathy, gastrointestinal hemorrhage, or infection at entry; d) serum bilirubin 10 mg/dl; e) prothrombin time 40%; f) platelet count 40.000/mm3; g) serum creatinine 2 mg/dl. The etiology of cirrhosis was postnecrotic and hepatitis B surface antigen-associated in all patients.

After admission to be hospital patients were given a diet containing 50 mEq/day of sodium. In patients with hyponatremia (serum sodium 130 mEq/L) water ingestion was restricted to 500 ml/day. During the first 5 days patients did not receive diuretics. On the fifth day a 24 h urine volume was collected to measure electrolytes. On the morning of the sixth day, blood samples were taken to measure serum electrolytes, blood urea nitrogen (BUN), serum creatinine, and standard liver function tests. Cardiac index was measured by doppler ultrasound (Toshiba SAI-5A). All these measurements were repated within the first 48h after the paracentesis and teratment of albumin. Methods used for these investigations have been previously described (20-22). The patients who were treated with paracentesis (4-12 lt until disappearance of ascites) and i. v. albumin was given in an amount enough to obtain the same volume of paracentesis. Paracentesis was performed under local anesthesia in the left lower abdominal quadrant.

Table I: Clinical data of the patients.

Age (year)	53.8 ± 4.5
Sex (F/M)	4/8
Cirrhosis (postnecrotic)	12
HBsAg+	12
Jaundice	5
Spider	7
Palmar erythema	10
Dupuytren contracture	3
Ginecomasty	2
Testicular atrophy	2
Umblical hernia	2
Splenomegaly	12
Pretibial edema	8

Tablo II: Laboratory values before and after large-volume paracentesis plus i. v. albumin infusion.

	Before	After	P
SBP (mmHg)	103.33 ± 5.41	103.75 ± 5.87	NS
DBP (mmHg)	65.83 ± 4.34	57.5 ± 1.79	0.01
Heart rate (min)	83.83 ± 2.49	83.83 ± 2.36	NS
Weight (kg)	72.33 ± 5.09	65.12 ± 4.74	0.06
Protrombin time (Sc)	22.25 ± 2.05	22.58 ± 1.95	NS
Parsial tromboplastin time (sc)	46.08 ± 2.65	44.66 ± 2.62	NS
Albumin (gr/dl)	2.59 ± 0.19	2.85 ± 0.10	0.02
Globulin (gr/dl)	4.38 ± 0.26	3.93 ± 0.31	0.03
Creatinin (mg/dl)	1.2 ± 0.12	0.96 ± 0.9	NS
BUN (mg/dl)	21.58 ± 3.53	17.5 ± 2.10	NS
Creatinin clerence (ml/dl)	77.71 ± 10.3	83.7 ± 9.94	NS
Serum sodium (mEq/L)	135.33 ± 2.43	134.25 ± 1.00	NS
Serum potassium (mEq/L)	3.78 ± 0.22	3.55 ± 0.11	NS
Hematocrit (%)	30 ± 1.08	28 ± 1.68	0.004
SGOT (U)	53.58 ± 9.54	41.58 ± 7.32	NS
SGPT (U)	36.83 ± 7.26	33.5 ± 4.69	NS
Bilirubin (mg/dl)	3.78 ± 1.28	3.04 ± 0.88	NS
EF (%)	61 ± 3.67	66 ± 2.30	0.007
CO (lt/min)	6.12 ± 0.72	5.87 ± 0.66	NS
CI (Co/m^2)	3.62 ± 0.39	3.58 ± 0.35	NS

SBP: Sistolic blood pressure
DBP: Diastolic blood pressure
EF: Ejection fraction
CO: Cardiac output
CI: Cardiac index

Once the needle entered the peritoneal cavity, the inner part was removed. The duration of most paracentesis ranged from 20 to 30 min. Samples of ascitic fluid were routinely taken during each paracentesis for cell count, biochemical examination, and cultures.

Serum creatinine, BUN, and serum and urine electrolytes were measured. Standard liver and renal function tests were measured at the and of treatment. Body weight and urine volume were determined daily in all patients.

Once ascites had disappeared, patients were discharged from the hospital with diuretics to prevent recurrence of ascites and were followed closely in the outpatient clinic. Patients in whom tense ascites developed during follow-up were readmitted to hospital and treated according to their initial schedule.

In analyzing complications during the first hospitalization, a patient was considered to develop renal impairment when there was a 50% increase in serum creatinine up to a level > 1.5 mg/dl, hyponatremia when there was a decrease in serum sodium > 5 mEq/L to a level below 130 mEq/L, and hyperkalemia when serum potassium increased > 1.5 mEq/L to a level above 5.5 mEq/L.

The analysis of the results were performed Student's t-test. Results were given as mean ± SEM.

RESULTS

Of the 12 patients 8 were men and 4 women. The mean age was 53.8 ± 4.5 years (range 35-83). The etiology of cirrhosis was postnecrotic and hepatitis B surface antigen associated in all patients. No patient associated with renal failure. Table 1 and 2 shows the clinic data, liver and renal function tests. The mean volume of ascites removed was 6.54 ± 1.3 liters (range 4-12) per patient. Albumin administration was 40.8 ± 3.9 gr (range 20-12). The mean paracentesis time was 235 ± 98.7 minutes (range 60-400). The mean loss of body weight was 7.21 ± 0.35 kg. Peripheral edema decreased markedly or resolved completely after treatment in all of the 8 pati-

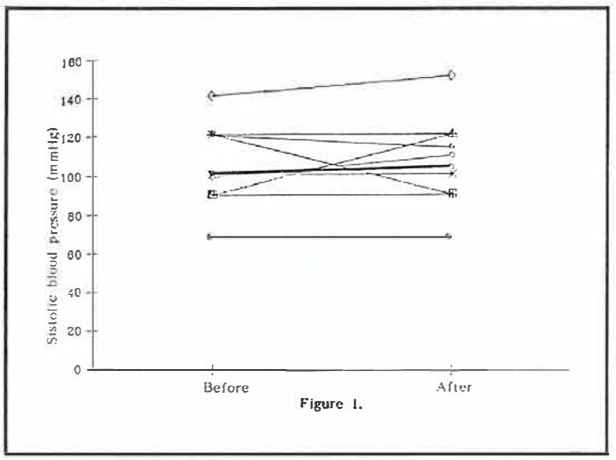


Figure 1. Systolic blood pressure values before and after large-volume paracentesis plus. i. v. albumin infusion.

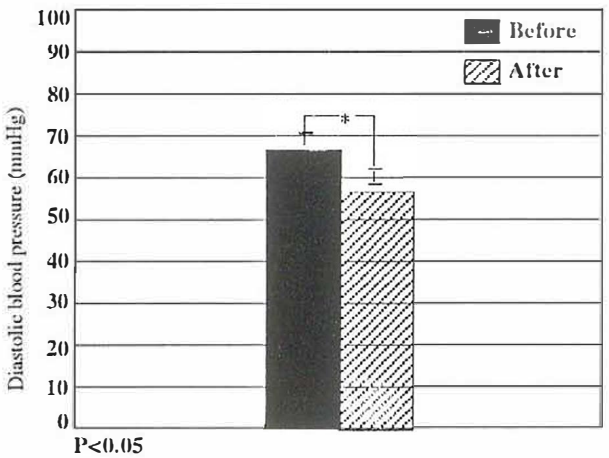
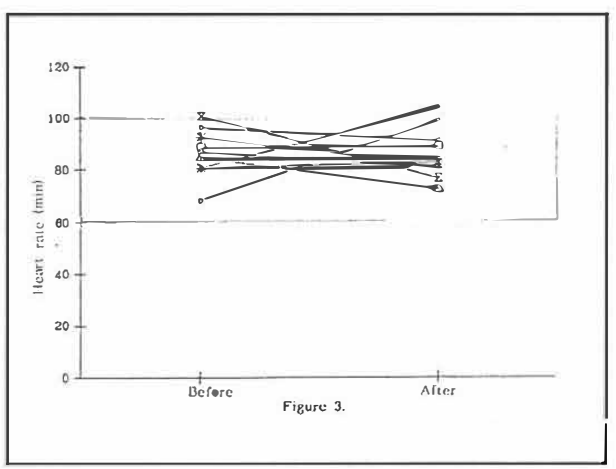


Figure 2. Diastolic blood pressure values before and after large-volume paracentesis plus i. v. albumin infusion.



Figur 3. Heart rate values before and after large-volume paracentesis plus i. v. albumin infusion.

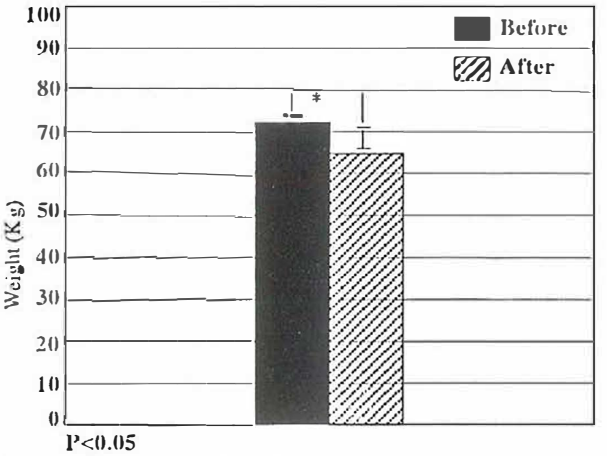


Figure 4. Weight values before and after large-volume parcentesis plus i. v. albumin infusion.

ents exhibiting it. There were no local complications related to the procedure in 11 patients. One patient ascite fluid leaked from the puncture hole for several hours after the parcentesis. After albumin administration increased in the hematocrite from30 ± 1.08 to 28 ± 1.68 ($p<0.004$), serum albumin from 2.59 ± 0.19 to 2.85 ± 0.10 gr ($p< 0.02$) and cardiac ejection fraction from 61 ± 3.67 to 66 ± 2.30 % ($p<0.007$). No significant changes were found in mean arterial pressure, heart rate, cardiac output and cardiac index at the end of the study. The body weight dropped significantly from 72.33 ± 5.09 to 65.12 ± 4.74kg ($p<0.006$). Serum sodium showed in two patients developed hyponatremia that required no treatment. After albumin administration decreased the mean diastolic blood pressure from 65.83 ± 4.34 to 57.5 ± 1.79 mmHg ($p< 0.01$). Renal and hepatic functions were measured after the administration of albumin and no significant changes were observed.

All of these results were demonstrated in figures1-16.

DISCUSSION

The results of the current study indicating that large-volume paracentesis associated with i. v. albumin infusion is a fast, effective, and safe method for the treatment of cirrhotics with tense ascites. This therapeutic procedure eliminated ascites in all patients. In addition, the in-

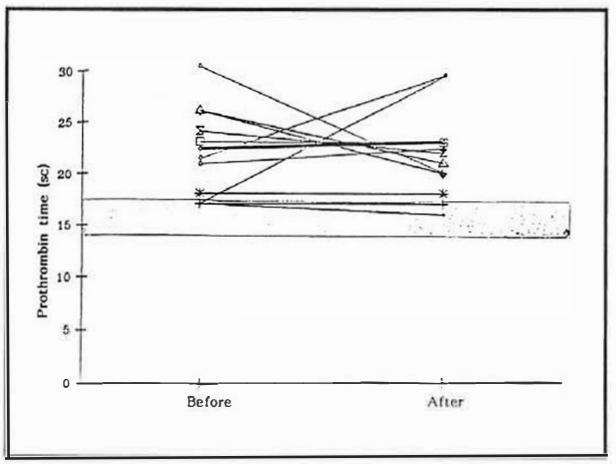


Figure 5. Protrombin time values before and after large-volume paracentesis plus i. v. albumin infusion.

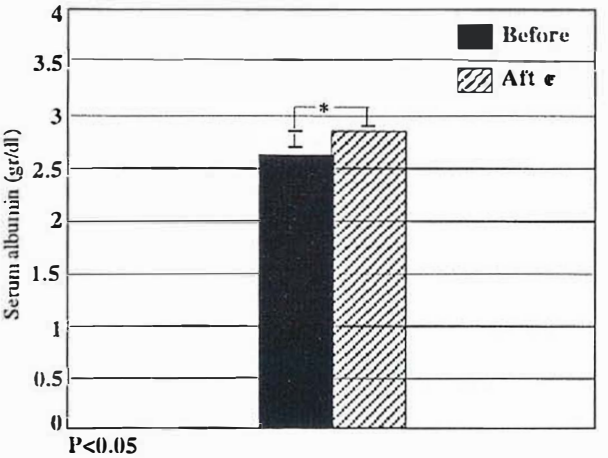


Figure 6. Serum albumin values before and after large-volume paracentesis plus i. v. albumin infusion.

cidence of complications in these patients was very much lower than that reported in previous studies in cirrhotic patients treated with diuretics (23). In addition, the duration of hospital stay was very short. The present study also confirms that paracentesis plus i. v. albumin does not impair renal hepatiç, cardiac function and is not associated with electrolyte deficiency. These findings support previous trials (16,19,25).

For many centuries paracentesis had been the only treatment that could be offered to patients with cirrhosis and ascites (26). This procedure, however, was abandoned about 30 yr ago concomitantly with the introduction of the modern diuretics. Reasons for this change were the effectiveness of these drugs in mobilizing ascites and the feeling that the abrupt decrease of intraabdominal pressure induced by decrease of intraabdominal pressure induced by large-volume paracentesis could be followed by a rapid reaccumulation of ascites, acute reduction of intravascular volume, renal failure, electrolyte disturbances, and hepatic encephalopathy (27). Several studies reporting the occurence of these complications in patients treated with paracentesis contributed to the progressive abandonment of the procedure (3,11-16,28). Currently, however, arguments against large-volume paracentesis do not appear as strong as in the past. The assumption that paracentesis adversely affects systemic hemodynamics and renal function

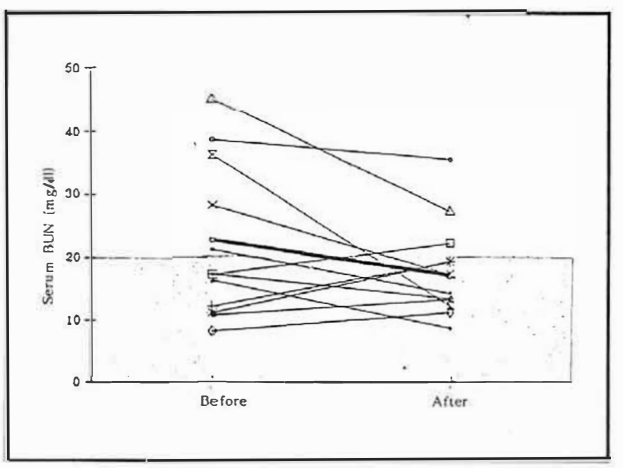


Figure 7. Serum BUN values before and after large-volume paracentesis plus i. v. albumin infusion.

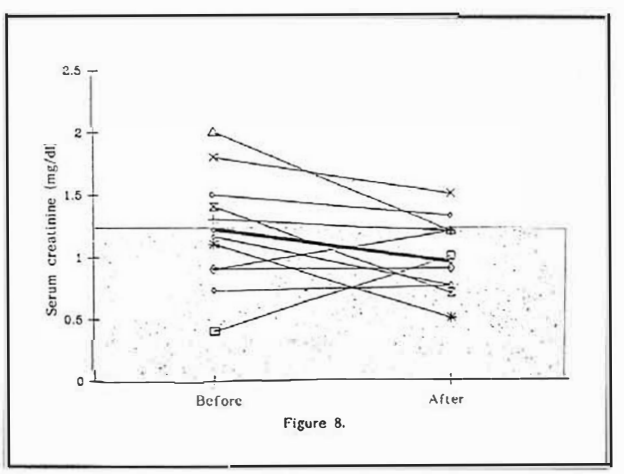


Figure 8. Serum creatinine values before and after large-volume paracentesis plus i. v. albumin infusion.

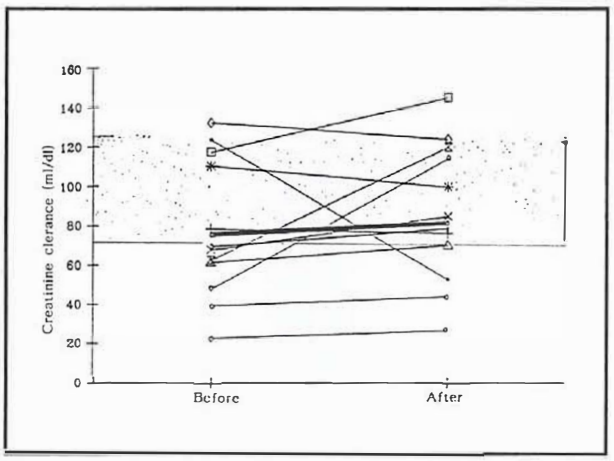


Figure 9. Creatinine clerence values before and after large-volume paracentesis plus i. v. albumin infusion.

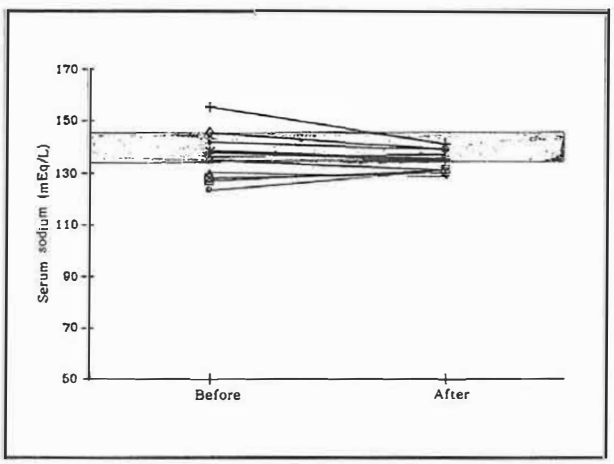


Figure 10: Serum sodium values before and after large-volume paracentesis plus i. v. albumin infusion.

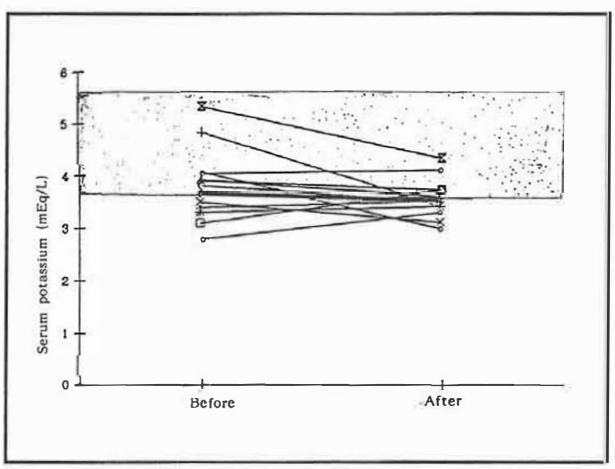


Figure 11: Serum potassium values before and after large-volume paracentesis plus i. v. albumin infusion.

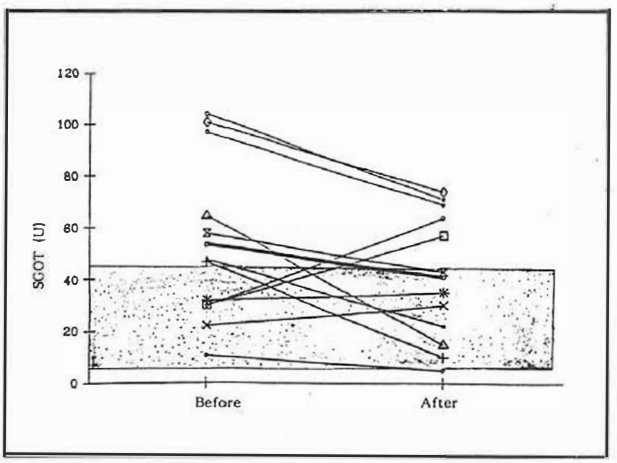


Figure 12: Serum SGOT values before and after large-volume paracentesis plus i. v. albumin infusion.

in patients with cirrhosis has never been substantiated by carefully controlled prospective investigations. Therefore, it is not clear whether complications originally attributed to paracentesis were caused by this procedure or by coincidental events. In fact, some investigations performed during the last three decades do not support the claim that large-volume paracentesis adversely affects systemic and renal hemodynamics in these patients (29-33).

At present some controlled trials have been published evaluating repeated large-volume paracentesis in the treatment of tense ascites in patients with cirrhosis (16,17,19,33,34). In the first study, Ginés et al. (17) compared paracentesis (4-6 L/day) until disappearance of ascites) plus i. v. albumin (40 g/day) with conventional diuretic treatment in 117 patients with cirrhosis admitted to the hospital for the treatment of an episode of ascites. They found that therapeutic paracentesis was more effective than diuretic treatment in the mobilization of ascites, that it was associated with a significantly lower incidence of hepatic encephalopathy and of renal and electrolyte disturbances, and that it significantly shortened the duration of hospital stay. In this study it was also shown that, contrary to the traditional concept, mobilization of ascites by paracentesis associated with i. v. albumin did not alter renal function or systemic hemodynamics, the latter being estimated either directly

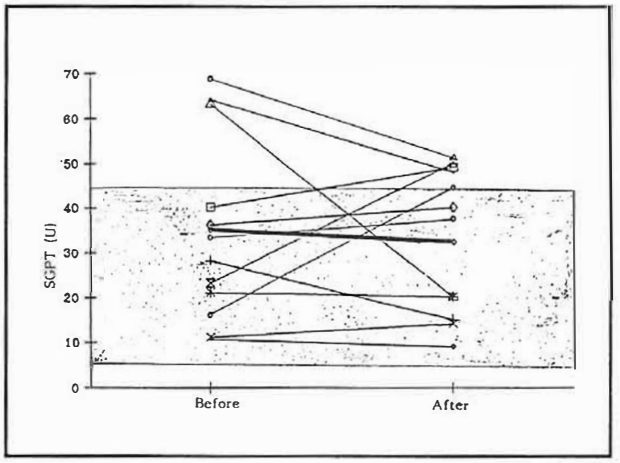


Figure 13: Serum SGPT values before and after large-volume paracentesis plus i. v. albumin infusion.

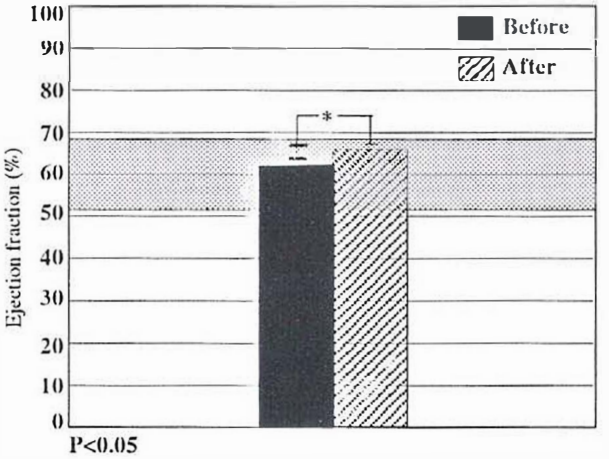


Figure 14: Ejection fraction values before and after large-volume paracentesis plus i. v. albumin infusion.

(by measuring plasma volume, cardiac output, and peripheral resistance) or indirectly (by measuring plasma renin activity and plasma norepinephrine and antidiuretic hormone concentrations). Subsequently, Salerno et al. (34) confirmed these findings in a randomized study including 41 patients. Finally, in a second randomized study comparing repeated large-volume paracentesis with and without albumin infusion in 105 cirrhotics, Ginés et al. (19) further confirmed the effectiveness and safety of repeated large-volume paracentesis plus i. v. albumin infusion in the management of cirrhotics with ascites and demonstrated that i. v. albumin infusion is an important measure in preventing deterioration of systemic hemodynamics and renal function after therapeutic paracentesis, as the mobilization of ascites in the group of patients not receiving albumin was associated with a marked increase in plasma renin activity in practically every patient, and with the development of renal impairment or dilutional hyponatremia, or both, in 20% of the cases. The occurrence of these renal and electrolyte disturbances was associated with a poor survival rate. A recent study by Simon et al.(35) in 13 patients with cirrhosis and ascites has confirmed that large-volume paracentesis without i. v. colloid replacement increase the activity of the renin-angiotensin system and impairs renal and systemic hemodynamics.

The results of the previous studies (17,20,36)

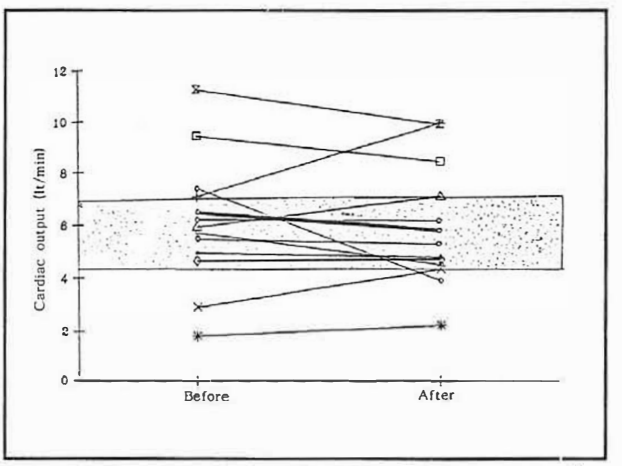


Figure 15: Cardiac output values before and after large-volume paracentesis plus i. v. albumin infusion.

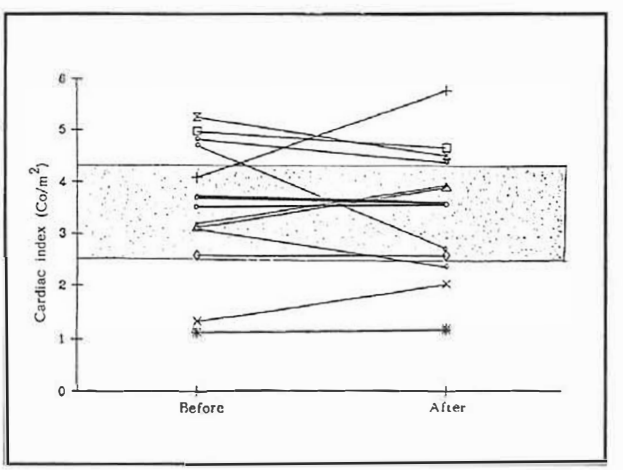


Figure 16: Cardiac index values before and after large-volume paracentesis plus i. v. albumin infusion.

should not be taken as an indication that therapeutic paracentesis is the treatment of choice for every patient with cirrhosis and ascites. Approximately 25% of these patients excrete relatively high amounts of sodium in the urine and their ascites may be lost simply by reducing sodium content in the diet (10). In other cirrhotic patients with ascites, sodium excretion is not high enough to allow the development of a negative sodium balance on a sodium-restricted diet; however, they easily respond when treated with low doses of diuretics (spironolactone alone or associated with a loop diuretic) (10). These two groups of patients are infrequently seen in hospitals, as they are satisfactorily managed with sodium restriction and low diuretic dosage on an outpatient basis. In according to these studies most cirrhotic patients admitted to the hospital for the treatment of ascites are ones who have developed tense ascites despite a standard diuretic treatment. It is this type of patient in whom therapeutic paracentesis is especially indicated, as strict sodium restriction and high diuretic dosage is required, therefore predisposing the patient to diuretic-induced complications.

In conclusion, our results indicate that tense ascites in cirrhosis can be completely mobilized within 1 or 2 h without adverse effects, providing the intravascular volume is expanded with human serum albumin. The subsequent administration of diuretics avoids reaccumulation of ascites in those patients responding to these drugs. Therefore, tense ascites in cirrhosis can be treated in a single-day hospitalization regime. Further studies are necessary to confirm our findings.

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