Research Article

Comparison of Low Dose Albumin Versus Full Dose Albumin in Improving Refractory Ascites in Cirrhotic Patients

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ABSTRACT

Background: Refractory ascites is one of the most important complications of cirrhosis & albumin is considered highly effective in controlling it.

Objective: To compare efficacy of 10g albumin versus 20g albumin in improving refractory ascites in cirrhotic patients.

Methods: This randomized control trial was conducted at department of Gastroenterology, Mayo hospital Lahore for 12 months. After ethical approval, 60 patients of chronic liver disease with refractory ascites were included in the study & were divided into two groups. Group A was administered with 20g albumin whereas; group B was given 10g albumin. Both groups were followed for next 3 days by measuring change in weight, abdominal girth and urine output. Data was analyzed by using SPSS v-21.

Results: There was no considerable difference between two groups regarding change in weight, abdominal girth and urine output. There was no significant difference in albumin response for both the groups in reducing ascites (p=0.6022).

Conclusion: Low dose albumin is as effective as full dose albumin for reducing refractory ascites among cirrhotic patients.

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Key Words: Low Dose Albumin, High Dose Albumin, Cirrhosis, Refractory Ascites, Comparison

Introduction:

Cirrhosis results from regenerative nodules and fibrosis in liver[1,2]. Ascites is an important marker of increase in portal pressure, liver function deterioration and worst prognosis in patients of cirrhosis by any etiology[3,4]. After development of ascites, mortality rate is expected to be 50% after 2 years[5]. In chronic liver disease (CLD), it is also included in most frequently occurring complications along with hepatocellular carcinoma[6,7].The pathogenesis of ascites is complex[4]. Development of ascites is the outcome of multiple factors, including arterial vasodilatation that impairs the renal blood flow[8,9], high sinusoidal capillary pressure secondary to portal hypertension (PHTN) and splanchnic vasodilatation from neurohumoral activation via mainly nitric oxide[9,10]. Hypoalbuminemia resulting from impaired hepatic synthetic function lower the oncotic pressure and aggravate fluid leakage into the third space[11,12]. Treatment of ascites in these patients should be done to improve discomfort, to relieve respiratory excursion, and to increase appetite because of disease's pressure effect and progression to spontaneous bacterial peritonitis(SBP)[13]. The management of uncomplicated ascites includes salt and water restriction and diuretics, and if it becomes complicated then liver transplantation, transjugular intrahepatic portosystemic shunting (TIPS) and therapeutic paracentesis are the available options[14,15,16]. The maximum accepted daily diuretic doses are 400 mg and 160 mg for spironolactone and furosemide respectively[17]. The efficiency of oral diuretics in the cure of massive cirrhotic ascites is reduced because of intestinal wall edema secondary to portal hypertension and hypoalbuminemia[18,19].

Additionally, impaired albumin function can alter albumin drug binding and may result in the abnormal bioavailability of diuretics[20]. Human albumin was found to enhance the response to diuretics and to reduce recurrence of ascites[21]. In this study, we evaluated efficacy of low dose versus high dose injectable human albumin along with oral diuretics in patients of cirrhosis with refractory ascites.

Objective:

To compare therapeutic effect of 10 gm versus 20gm albumin in treatment of refractory ascites due to cirrhosis.

Methods:

This randomized clinical trial was conducted at Department of Gastroenterology, King Edward Medical University, Mayo Hospital, Lahore from December 2017 to November 2018. After ethical approval of the study, 60 diagnosed patients of cirrhosis (undersized and nodular liver with augmented echogenicity and asymmetrically appearing areas on ultrasonography) of age 20-70 years with either gender presenting with refractory ascites (Failure to respond to spironolactone 400mg/day; furosemide 160mg/day and water restriction to 1.0 L/day) were included in the study by simple random type probability sampling. The baseline albumin of the patients was ≤2.0 to 2.5 mg /dl. Patients with metastatic hepatocellular carcinoma, portal vein thrombosis, ongoing bacterial infection & cardio-pulmonary failure were excluded from the study. Sample size was calculated as 5% level of significance, 90% power of test with expected mean value albumin low dose 128±287.62 and albumin full dose 468±324[20]. Demographics such as gender, age, and disease duration were noted for each patient. Informed written consent was taken from all patients. On day of admission complete blood count, liver & kidney functions test, prothrombin & activated partial prothrombin time, Urine CE, Ascitic fluid analysis tests were sent to college pathology laboratory. Then the patients were divided into two groups by simple Lottery (Bingo) method. In group A, patients were given albumin 20 g (100 ml) and in group B, patients were given albumin 10 g (50ml) for three consecutive days. Patients of both groups received full dose of diuretics during the study. Albumin effectiveness was checked by monitoring decrease in daily weight (0.5-1kg/day), abdominal girth and increase urine output (a negative fluid balance of 500-1000 ml/day) and was recorded in pre-designed proforma.

SPSS v.21 was used to analyze the collected data. Means and standard deviations were used to represent quantitative variables such as age, whereas, qualitative variables like gender and albumin response are presented as frequency and percentage. Low dose albumin and full dose albumin groups are compared for response of albumin infusion by using independent t-test (sample) with -p-value≤0.05.

Results:

The mean age for group A was 51.57 ± 11.30 years, whereas, for group B it was 53.50 ± 10.74 years. Majority of the patients (31.66%) had age range from 51 to 60 years, followed by age groups 41-50 years (21.66%), 61-70 years (16.66%), 20-30 years (15%) and 31-40 years (15%). Out of 60 patients in our study, there were 30 males & 30 females. The t-test value was 0.679, whereas, p value was 0.5. This indicates an insignificant relation between age and albumin response (Table-1).

Table 1: *Age distribution in both study groups*

Age	Study groups	Mean	S.D	Minimum	Maximum	p-value
Age (years)	*20 gm Albumin*	51.57	11.30	22	70	0.5
	10 gm Albumin	53.50	10.74	29	70	
	Total	52.53	10.97	22	70	

Among the characteristics, weight change was recorded at day 3 in both groups. Minimum value noted was 29.6kg & maximum value was 87.5kg for both groups. The p values for all the weight change showed insignificant difference (p>0.05).Change in abdominal girth at day 3 was also noted & minimum was 30.8cm & maximum 42.6cm in both groups. The p value (<0.05) at day 3 show significant difference of abdominal girth bet-

Table 2: *Change in characteristics in Group A& B after 3 days albumin infusion*

Parameters	Study groups	Mean	S.D	Minimum	Maximum	p-value
Change in weight (kg)	*20 gm Albumin*	59.41	13.19	29.6	87.5	0.341
	10 gm Albumin	56.40	10.99	38.0	79.0	
	Total	57.91	12.13	29.6	87.5	
Change in Abdominal Girth (cm)	*20 gm Albumin*	34.55	2.35	30.8	42.6	0.001*
	10 gm Albumin	34.56	2.50	31.5	40.4	
	Total	34.55	2.40	30.8	42.6	
Change in Urine output(ml)	*20 gm Albumin*	1360.66	298.03	49.8	2000.0	0.001*
	10 gm Albumin	1023.08	431.12	36.0	1480.0	
	Total	1191.87	404.95	36.0	2000.0	

ween the study groups. Change in urine output at day 3 showed minimum values as 36ml & maximum as 2000ml for both the study groups. The p value calculated for difference of urine output at 3rd day was significant ($p<0.05$) (Table 2).

Albumin response from both the groups showed high dose group as 93.33% response in comparison to 96.66% response from low dose group. The t test value was 0.0622, which indicates an insignificant difference between the two albumin groups (Table 3).

Table 3: *Albumin response in Group A& B*

Study groups	Albumin response	T test
Group A (high dose albumin)	28 (93.33%)	0.0622
Group B (low dose albumin)	29 (96.66%)	

Discussion:

In this study we observed change in weight, abdominal girth and urine output after 3 days of both low dose versus full dose albumin treatment groups in cirrhotic patients with refractory ascites & it was found that low dose albumin (10g) is as effective as full dose (20g) albumin. Previous literature have reported that albumin bring about improvement in diuretic response in cirrhotic patients with hypoalbuminimia however different doses of albumin have not been studied much.[1] Alsebaey A et al found out that low-dose albumin was comparable to the standard-dose albumin for the prevention of paracentesis-induced circulatory dysfunction (PICD) in patients of CLD with refractory ascities[22]. This was the same result as we found in our study.

On the other hand Tajiri K et al established contradictory to our study that the effectiveness of long-term albumin administration of high dose more than 40 g per week may improve survival in patients with decompensated cirrhosis with refractory ascites[23].

In another study it was found that in patients with cirrhosis and refractory ascites, long-term treatment with albumin improves survival and reduces the probability of emergent hospitalizations however no dosage comparison was done[24]. In PRECIOSA study done on a very small sample size of 18 showed that long-term (12 weeks) high-dose albumin of 1.5 g/kg of body weight/week normalized serum albumin concentration as compared to the dose of 1 g/kg body weight every 2 weeks and hence reduced systemic inflammation and circulatory dysfunction in patients with decompensated cirrhosis with refractory ascites[25].

Although literature has extensive studies discussing benefits of albumin, the effect of the different doses of albumin has not been elaborated much in most of the research work. The main strength of our study was a novel work that we studied the efficacy of 10g & 20g albumin for controlling refractory ascites in cirrhotic patients for relatively larger sample size, so that we may use it as a reference in future. It will be cost effective & lesser chance of complications in these patients. However single centered study, short follow up & limited time and resources were the major limitations of our study.

Conclusion:

It was concluded that significant difference was noted

between both the high dose group and low dose group in terms of change in weight, abdominal girth, and urine output. However, the albumin responses for both the groups were same. Hence low dose (10g) albumin is as effectiveness as full dose (20g) albumin in addressing refractory ascites among cirrhotic patients. In future we will advise physicians & gastroenterologists to recommend low dose albumin to reduce the cost of patient treatment in order to get the same response & hence lesser risk of complications & hospital admissions.

Ethical Approval: Given

Conflict of Interest: The authors declare no conflict of interest.

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