Original Article

Effect of conventional diuretics versus conventional diuretics plus mannitol on electrolytes for the treatment of cirrhotic ascites

Alam MJ[1], Ashraf MS[2], Aktar MN[3], Sharmin S[4], Das DC[5], Ferdoushi S[6], Sarker MJA[7]

Abstract

Ascites is the most frequent finding of decompensated liver cirrhosis. Mannitol may be used with conventional diuretics for increase urinary volume for the treatment of cirrhotic ascites. This case control study was done in the Department of Medicine, Sere-Bangla Medical College &Hospital, Barisal from July 2009 to June 2011. No electrolyte imbalance was seen by conventional diuretics plus mannitol for the treatment of cirrhotic ascites. Mannitol did not causee lectrolyte imbalance & may be used with conventional diuretics for the treatment of cirrhotic ascites as it increased the urinary volume.

Key words: Cirrhosis, ascites, conventional diuretics, mannitol

Introduction

Cirrhosis is one of the leading causeof death in Bangladesh. Clinically cirrhosis of liver are 2 types e.g. compensated & decompensated cirrhosis. Signs of decompensation are jaundice, ascites, encephalopathy and variceal bleeding. Etiology of cirrhosis of liver are chronic hepatitis B, chronic hepatitis C, alcoholic hepatitis, drug induced hepatitis, NASH, autoimmune hepatitis, Wilson's disease & cryptogenic hepatitis. In our country common etiological causes of cirrhosis is chronic hepatitis B & chronic hepatitis C. Pathologically cirrhosis of liver may be defined as degeneration of normal architecture of liver with appearance of nodules in the liver. Among decompensated cirrhosis of liver, ascites is the commonest manifestation; only 50% patients survive for 2 years.[1]

A cirrhotic patient treated with diuretics may develop electrolyte imbalance such as hyponatraemia, hypokalaemia etc. The condition of the patient may deteriorate due to electrolyte imbalance.

Ascites is the excess accumulation of free fluid in the peritoneal cavity. Ascites may be mild, moderate & severe. In severe ascites with respiratory distress there is indication of aspiration. When there is ascites, cirrhosis of liver usually accompanies the signs of portal hypertension. Signs of portal hypertension are splenomegaly, caput medusa, oesophageal & rectal varices.[2]

Standard therapy for cirrhotic ascites is restriction of salt intake & use of diuretics. Approximately 90% of patients show response to initial oral diuretic therapy.[3] Massive diuresis by oral diuretics may causes renal dysfunction, electrolytes disorder & hepatic encephalopathy.[4]

Twenty percent of patients responding to initial oral diuretic become resistant to them with time.[5] At this stage, the patient may have liver failure & volume loss resulting from diuretic therapy. There may develop hepatorenal syndrome. In patients with decompensated cirrhosis with ascites in whom response to diuretics is insufficient & in whom therapy dependant complications have developed, use of standard diuretics should be with caution and additive treatment modalities are needed in these cases.[2]

Additive e.g. mannitol is an osmotic diuretic, is pharmacologically inert substance, can be filtered in glomerular filtrate, not reabsorbed in renal tubules, so produce diuresis.[6] It can be used in clinical practice in patients with ascites, as an additive to diuretics, but there are

1. Dr Md Jamshed Alam, Associate Professor & Head, Department of Hepatology, Shaheed Suhrawardy Medical College Hospital, Dhaka.
2. *Dr Mohammad Shahed Ashraf, Assistant Professor Department of Hepatology, Shaheed Suhrawardy Medical College Hospital, Dhaka. Email: shahedashraf@ymail.com
3. Dr Mst Nurunnahar Aktar, Assistant Professor, Department of Obstetrics & Gynaecology, Shaheed Suhrawardy Medical College Hospital, Dhaka.
4. Dr Sadia Sharmin, Resident, Department of Oncology BSMMU, Dhaka
5. Dr Dulal Chandra Das, Medical Officer, Department of Hepatology, BSMMU, Dhaka
6. Dr Sheuly Ferdoushi, Medical Officer, Department of Clinical Pathology, BSMMU, Dhaka
7. Dr Md Jahangir Alam Sarker, Assistant Professor, Department of Hepatology, Shaheed Suhrawardy Medical College Hospital, Dhaka

For correspondence

a few controlled studies on its efficacy. It acts on proximal convoluted tubule, limbs of loop of Henle & partly act on collecting tubule.[7] It blocks the reabsorption of water at the proximal convoluted tubule & limbs of loop of Henle & causing water diuresis. Because of increase water dieresis[6], the contact period between sodium & tubular epithelium is decreased, so less sodium reabsorption leads to natriuresis.[7]

In this study, we aimed to evaluate the effect of mannitol infusion of short duration (3 days) on diuretics therapy in cirrhotic patients with ascites who are using conventional diuretics. Conventional diuretics means usual diuretic in the treatment of cirrhotic ascites (frusemide& spironolactone in the ratio of 1: 2.5).

Electrolyte are important component of blood. Electrolytes are serum sodium, serum potassium, serum chloride & serum bicarbonate. Normal value of serum sodium is 135-145 mmol/L, serum potassium is 3.5- 5.5 mmol/L, serum chloride is 98- 107 mmol/L & serum bicarbonate is 23- 28 mmol/L. There may be development of electrolyte imbalance such as hyponatraemia, hypokalaemia etc. by use of diuretics.

Short term mannitol therapy may make a significant contribution to diuretic therapy without electrolytes imbalance, it may be used as an additive to conventional diuretics in the treatment of cirrhotic ascites.

Methods

It was a case control study. It was done in the department of Medicine,Sere-Bangla Medical College & Hospital, Barisal from July 2009 to June 2011. Total 100 patients of cirrhosis of liver with ascites were included in this study. Cirrhotic patients with ascites of either sex aged 18 years or more, on conventional diuretics for at least 5 days were included in the study.

Both cases & controls were taken randomly based on prefixed inclusion & exclusion criteria. 50 patients were taken as cases & 50 were controls. Infusion of 20% mannitol was given to the cases & Infusion of 5% D/A to the controls.

Diagnosis of cirrhosis with ascites was done on clinical, biochemical, ultrasonographic & endoscopic evidence. Patients with endoscopic proven oesophageal varices & USG evidence of coarse liver with ascites were included in this study.

Results

Base line clinical & laboratory data in the study group showed that average age (years) 44± 23. Number of male patients were 60 & female patients were 40. Etiologically 75 cases were HBV related cirrhosis, 15 cases HCV related cirrhosis & 10 were NBNC related cirrhosis.

Serum bilirubin ranges from 70±50 (micromol/l), ALT 90± 62 (u/l), alkaline phosphatase 200± 155 (u/l), PT 26 ±12(s), urea 29 ±9 (mg/dl), creatinine 1.3± 0.7 (mg/dl), albumin 24 ±10 (gm/l), serum sodium 126± 8 (mmol/l), serum potassium 4.5± 1.0 (mmol/l), serum chloride 100± 4(mmol/l), bicarbonate 24 ±2 (mmol/l).24 hours urinary sodium 80 ± 50 (mmol/l), urinary volume 1675± 1175 (ml/d), weight 68± 27 (kg).(Table-I)

Table- I: Base line clinical & laboratory data

	Mean ± SD
Age (year)	44± 23
Male	60
Female	40
Causes of cirrhosis: Hepatitis B	75
Hepatitis C	15
NBNC	10
Serum bilirubin(micromol/l)	70 ±50
alkaline phosphatase (u/l),	200 ±155
ALT (u/l)	90 ± 62
Prothrombin time(s)	26± 12
Serum urea (mg/dl)	29 ±9
Serum creatinine (mg/dl)	1.3 ±0.7
Serum albumin (gm/l)	24 ±10
Serum sodium(mmol/l)	126± 8
Serum potassium (mmol/l)	4.5± 1.0
Serum bicarbonate (mmol/l)	24 ±2
Serum chloride (mmol/l)	100± 4
Urinary sodium(mmol/l)	80 ±50
Urinary volume (ml/d)	1675± 1175
Weight (kg)	68 ± 27

There was significant difference of urinary volume before & after 20%mannitol infusion but there were no significant difference of 24 hours urinary sodium, weight, serum albumin, serum urea, serum creatinine, serum sodium, serum potassium, serum chloride & serum bicarbonate level before & after 20% mannitol infusion. (Table- II).

Table-II: Clinical & Laboratory parameters before & after 20% mannitol infusion

	Before mannitol infusion (mean ±SD)	After mannitol infusion (mean ±SD)	SD	t	P	Remarks
Urinary volume	1300± 470	1800± 490	454.65	4.3	<0.05	Significant
Urinary sodium	61.6± 28.6	66.7 ±42.4	36.16	0.55	>0.05	Not significant
Weight	57.7 ± 112.5	55 ± 11.5	12.47	0.62	>0.05	Not significant
Serum albumin	23.5 ± 5.06	24.4 55 ± 4.72	4.85	0.72	>0.05	Not significant
Serum urea	26.2± 5.2	26.3± 5.8	5.5	0.07	>0.05	Not significant
Serum creatinine	0.95± 0.29	1.03 ±0.33	0.31	0.62	>0.05	Not significant
Serum sodium	129.1± 5.82	130.5± 6.11	5.95	0.65	>0.05	Not significant
Serum potassium	4.2± 0.50	4.3±0.70	0.61	0.63	>0.05	Not significant
Serum chloride	100 ±3	101 ±3	4.85	0.57	>0.05	Not significant
Serum bicarbonate	25±2	25±3	2.85	0.56	>0.05	Not significant

There were no significant difference among 24 hours urinary volume(ml/day), 24 hours urinary sodium(mmol/l), weight(kg), serum albumin(gm/l), serum urea(mg/dl), serum creatinine(mg/dl), serum sodium(mmol/l), serum potassium(mmol/l), serum chloride(mmol/l) & serum bicarbonate(mmol/l) before & after 5% D/A infusion. (Table -III)

Table-III : Clinical & laboratory parameters before & after 5% dextrose infusion

	Before 5% D/A infusion (mean±SD)	After 5% D/A infusion (mean ±SD)	SD	t	P	Remarks
Urinary volume	1480± 490	1360± 615	454.30	0.5	>0.05	Not significant
Urinary sodium	59± 20.9	59 ±20.8	32.39	0.05	>0.05	Not significant
Weight	53.86 ± 6.9	53.4 ± 7.2	7.06	0.18	>0.05	Not significant
Serum albumin	23.6 ± 5.5	26.3 ± 5.4	5.44	1.35	>0.05	Not significant
Serum urea	26.2± 5.2	26.3± 5.8	5.5	0.07	>0.05	Not significant
Serum creatinine	1.12± 0.24	1.08 ±0.19	0.21	0.57	>0.05	Not significant
Serum sodium	132.7± 5.94	132.4± 5.84	5.89	0.15	>0.05	Not significant
serum potassium	3.08± 0.89	3.86±0.57	0.74	0.07	>0.05	Not significant
Serum chloride	100 ±3	101 ±3	4.85	0.57	>0.05	Not significant
Serum bicarbonate	25±2	25±3	2.65	0.56	>0.05	Not significant

There were significant difference of 24 hours urinary volume(ml/day) after 20% Mannitol infusion in compared to 5% D/A infusion ($p<0.05$). (Table- IV)

Table-IV: Comparison of urinary volume (ml/day) in control & study cases

	Control (mean SD)	Case (mean SD)	SD	t	P	Remarks
Urinary volume Before 5% D/A infusion for control & 20% mannitol for case	1480± 490	1300± 470	480.1	0.51	>0.05	Not significant
Urinary volume after 5% D/A infusion for control & 20% mannitol for case	1360± 615	1800± 439	534.3	3.18	<0.05	Significant

The study showed that urinary volume was significantly increased after 20% Mannitol infusion along witha conventional diuretics without any electrolyte imbalance.

Discussion

The effect of mannitol infusion on the response to diuretic therapy in cirrhotic patients with ascites was studied in the Department of Internal Medicine, University of Istambul,Turkey by Pamuk&Sonsuz.[8] They had taken total 30 patients & divided into two groups. The first group (10 males & 5 females, mean age 55.2 years) was given 100 ml 20% mannitol infusion, whereas the second group (11 males, 4 females, , mean age 55.7 years) was given 100 ml 5% D/A infusion. Both the groups received the conventional diuretics. In the mannitol group urinary volume increased in 12 patients & increase in urinary Na excretion was observed. In the control group urinary volume increased in 3 patients & Na excretion increased in 6 patients, urinary volume decreased in 5 patient & daily Na excretion decreased in 9 patients. Daily urinary volume did not change in 7 patients with 5% D/A infusion. In the control group, the change in the mean daily urinary volume & Na excretion was not significant ($p>0.05$). A similar study "Refractory ascites, Modulation atrial natriuretic factor unresponsiveness by mannitol' was done by Morali, Tobe & Skorce[1] in the University of Toronto, Canada. They attempted to decrease the proximal reabsorption of sodium with mannitol in patients unresponsive to atrial natriuretic factor. They studied 10 patients with resistant ascites in whom diuretic was withheld & plod on 20 mmol/day sodium diet for 7 days. The next day all patients received an infusion of 40 gm of mannitol & subsequently a combined infusion of mannitol& atrial natriuretic factor. They showed that 6 patients responded to mannitol alone with an increased diuresis &natriuresis ($p<0.05$), whereas 4 did not (non-responders). The combination of atrial natriuretic factor & mannitolinduced a further significant increase in Na excretion but there was no increase in urine output compared with mannitol alone.

In the present study100 cirrhotic patients with ascites (50 were cases & 50 were controls) were getting conventional diuretics were included in this study. All patients were treated with a combination of frusemide & spironolactone in various doses.The dose of diuretics was constantfor at least 5 days before the 1st day. Patients urine were collected for 24 hours urinary volume & urinary sodium excretion. Blood samples were taken for serum albumin, urea, creatinine, sodium, potassium, chloride & bicarbonate levels. Patients were randomly divided into two groups (50 were cases & 50 were controls). Patients in both groups were similar in age, sex, biochemical parameters, predictive of severity of liver diseases. A dose of 100 ml 20% mannitol was given I/V to the case group & 100 ml 5% D/A to control group for consecutive 3 days. Patients of both groups also given diuretics every day at the same previous dose. The following morning after each day 24 hours urine output was measured & weight of the patients were recorded for consecutive 2 days. On the 3rd day weight of the patients, 24 hours urinary volumes & 24 hours urinary sodium excretion was measured. Blood was collected for serum urea, creatinine, albumin, sodium, potassium, chloride & bicarbonate levels. In this study, mannitol significantly increased the urinary output without electrolytes imbalance when used along with conventional diuretics. It provided comfort to the patients with cirrhotic ascites by reducing ascites but did not produce electrolytes imbalance.

Use of mannitol as an additive to conventional diuretics in the treatment of cirrhotic ascites was safe, available, well tolerated & cost effective. Mannitol increased the urinary output in cirrhotic patients with ascites without electrolytes imbalance.

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