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COMPARISON OF ORAL MIDODRINE AND ALBUMIN INFUSION IN CIRRHOTIC PATIENTS WITH REFRACTORY ASCITES UNDERGOING LARGE-VOLUME PARACENTESIS

Medicine

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ABSTRACT

Introduction: One frequent cirrhosis consequence that is linked to higher morbidity and death rates is ascites. For cirrhotic patients with tight ascites, albumin infusion has been the conventional therapy to avoid circulatory dysfunction following paracentesis. But because of its expensive cost, researchers are looking at other affordable options like vasoconstrictors. The perfusion of the kidneys and the amount of blood in circulation have both been effectively increased by midodrine. In order to assess the effects of midodrine vs albumin infusion in cirrhotic patients having large-volume paracentesis (LVP) for refractory ascites, this research was conducted. **Methodology:** This study involved the random prescription of either albumin infusion, oral midodrine for 7 days, or oral midodrine for 30 days after LVP to a total of 90 cirrhotic patients with refractory ascites. Statistical comparisons were made between the short- and long-term death rates, treatment costs, changes in systemic and portal hemodynamics, and the onset of hyponatremia or renal impairment. **Results:** Group M30 showed superior outcomes compared to Group A and Group M2 across various parameters. Notably, it showed the most favourable changes in mean arterial pressure, serum sodium levels, urinary sodium excretion, 24-hour urinary volume, portal vein flow volume, and creatinine clearance, all statistically significant ($p<0.0001$*). These results suggest that prolonged midodrine intake may offer better improvements in haemodynamics, renal function, and portal vein flow volume compared to shorter duration midodrine intake or albumin infusion. **Conclusion:** When cirrhotic patients with refractory ascites undergo LVP, midodrine shows similar effectiveness to albumin infusion in reducing morbidity and death, while being more cost-effective. Prolonged midodrine intake appears to offer additional benefits in terms of improving the perfusion of kidneys and natriuresis.

KEYWORDS

Cirrhosis, Ascites, Large-volume paracentesis, Midodrine, Albumin infusion, Renal perfusion

INTRODUCTION

Cirrhosis stands as a persistent liver condition characterized by extensive liver tissue damage, involving fibrosis and nodular regeneration. [1] The impact of cirrhosis and its associated complications, collectively termed as chronic liver diseases (CLDs), on mortality rates in India has witnessed a steady rise since 1980. In contrast, China, another populous country in Asia, has seen relatively stable rates, with some indications of a downward trend. [2] Ascites emerges as a frequent complication accompanying liver cirrhosis. Initial presentation reveals ascites in approximately 20% of cirrhosis patients, with a distressing 20% mortality rate within the inaugural year following diagnosis. [3] Refractory ascites, per the International Ascites Club, resists mobilization or recurs post-large-volume paracentesis despite medical intervention. [4] Sodium retention in cirrhosis stems from heightened tubular reabsorption. [5] A moderately restricted salt diet (5–6.5 g/day) is advised, as drastic reductions may lead to complications and mortality, posing compliance challenges. [6] Large volume paracentesis (LVP) represents the primary therapeutic approach for addressing substantial volume ascites, utilized either concurrently with diuretic therapy to alleviate symptoms associated with abdominal distension, or independently in cases of refractory ascites where diuretics fail to yield efficacy or their usage is untenable due to adverse effects. [7,8] The implementation of therapeutic paracentesis alongside plasma volume augmentation utilizing albumin stands as a viable and secure procedure, presenting fewer risks compared to diuretic therapy in these scenarios. However, the utilization of albumin poses challenges due to its high cost and potential risk of disease transmission, thereby engendering controversy in certain nations. [9-11] Midodrine hydrochloride gives rise to an active metabolite known as desglymidodrine, which functions as an alpha1-agonist. Its mechanism of action involves the activation of alpha-adrenergic receptors in the venous and arteriolar arteries, which results in elevated blood pressure and vascular tone [12] The utilization of vasopressors such as midodrine in non-azotemic patients afflicted with ascites has yielded diverse outcomes. These interventions have yielded conflicting findings regarding their effect on natriuresis and mean arterial pressure, as well as significantly lower levels of aldosterone and plasma renin. [13] Midodrine may be just as effective as albumin in avoiding post-paracentesis circulatory dysfunction (PICD) in individuals with cirrhosis, according to a prior research. [10] On the other hand, an intravenous albumin injection proved to be more efficacious than a set, short-term dosage of midodrine in another trial. [9] In order to examine the effectiveness and safety of midodrine and albumin in patients after liver venoplaston surgery (LVP) who had refractory ascites and liver cirrhosis, this research was conducted.

MATERIAL AND METHODS

According to inclusion-exclusion criteria, 90 patients with liver cirrhosis and refractory ascites were included in this trial, which took place between July 2022 and April 2024. Ninety patients who satisfied the study's inclusion requirements were enrolled once the ethical clearance and informed permission were obtained. Patients eligible for inclusion in this study were those diagnosed with cirrhosis presenting with refractory or recurrent ascites, aged between 18 and 70 years, and free from sepsis. Additionally, inclusion criteria required a prothrombin concentration exceeding 30% and a platelet count exceeding 25,000/l, alongside a serum creatinine level below 1.5 mg/dl. Exclusion criteria encompassed recent alterations in diuretic dosage within 7 days before enrolment, recent cases of gastrointestinal bleeding or spontaneous bacterial peritonitis that occurred within the same time period, severe respiratory distress necessitating immediate paracentesis, the existence of cancer or hepatic encephalopathy, uncontrolled diabetes (HbA1c >8.5%), arterial hypertension, a history of heart failure or coronary heart disease, or a patient who declines to take part in the study.

Patients were hospitalized for a work-up preparation day prior to paracentesis. Day 0 of the paracentesis was designated. Once informed written consent was obtained, patients were assigned to one of three groups using the alternating assignment method: Group A: Following large volume paracentesis, 30 patients received a normal dosage of albumin (8 g for each liter of ascitic fluid removed). Group M2 (2-Day Midodrine Group): In the seven days following high volume paracentesis, 30 patients received 12.5 mg of midodrine every eight hours.

Group M30 (30 Days Midodrine Group): During 30 days following LVP, 30 patients got 12.5 mg of midodrine every 8 hours. Furthermore, under stringent aseptic settings and local anesthesia, LVP required the evacuation of five liters or more of ascitic fluid. Blood pressure was tracked, and paracentesis was stopped if arterial blood pressure fell

20% from the first reading or if, upon adjustments, the cannula stopped draining ascitic fluid. All patients had clinical and analytical evaluations on days 7 and 30 following LVP. Clinical follow-up was conducted on patients from day 7 to day 30 to monitor any significant adverse events. The development of hyponatremia or renal impairment following high volume paracentesis was the primary outcome. Indicators of post-paracentesis circulatory dysfunction (PICD) included alterations in systemic and portal hemodynamics, which were secondary outcomes. Serum creatinine elevated beyond 1.5 mg/dl (>50% rise from baseline) is considered renal impairment. Patients with initial serum sodium levels >130 mEq/l are classified as having a reduction of >5 mEq/l to <130 mEq/l. Similarly, patients with starting serum sodium levels <130 mEq/l are defined as having a decrease of >5 mEq/l after paracentesis.

Statistical Analysis:
The study's data were statistically analyzed using SPSS version 20.0, with a p-value of 0.05 being utilized as the significance threshold. The data were presented as frequency for categorical variables and mean ± standard deviation for continuous variables. Chi square statistical analysis was used for categorical data, and ANOVA and the student's t-test were used for continuous data.

RESULTS

The study compares three groups of patients (Group A, Group M2, Group M30) with liver cirrhosis across various clinical characteristics. The results show no significant differences in age, gender, BMI, etiology of liver cirrhosis, Child-Pugh classification, diuretic use, history of previous tapping, volume of ascites removed, sodium levels, creatinine, urinary sodium, urinary volume, and renal artery resistive indices among the groups. However, significant differences were observed in mean arterial pressure (MAP) (p=0.0032) and portal vein (PV) flow volume (p=0.0003), indicating these parameters were notably different between the groups, with MAP being lower and PV flow volume higher in Group M30. These findings suggest that while many characteristics are similar across the groups, MAP and PV flow volume differ, potentially highlighting different hemodynamic profiles or responses to treatment. [Table 1; Fig 1 and 2] At sixth day, in Group A, significant changes included decreased diastolic BP (p=0.0266), heart rate (p<0.0001), increased serum sodium (p=0.0037), and portal vein flow volume (p=0.0005). Group M2 showed improved heart rate (p=0.0031), portal vein flow (p<0.0001), urinary sodium (p<0.0001*), serum creatinine (p=0.0009), and decreased creatinine clearance (p=0.0064). In Group M30, there were reductions in systolic BP (p=0.0026), heart rate (p=0.01166), and increased urinary sodium (p<0.0001), as well as significant changes in portal vein flow volume (p=0.0326). MAP and renal artery indices showed no significant changes in any group. Ejection fraction improved only in Group A (p=0.0313). [Table 2] At 30 days, significant improvements were observed in the following parameters: heart rate (p<0.0001*), urine volume (p<0.0001*), creatinine clearance (p<0.0001*), ejection fraction (p<0.0001*), mean arterial pressure (p=0.0004*), systolic blood pressure (p=0.0366*), diastolic blood pressure (p<0.0001*), and heart rate (p<0.0001*). Serum creatinine and renal parameters, however, did not alter considerably. In Group M2, similar improvements were noted in heart rate, serum sodium, urinary volume, urinary sodium, creatinine clearance, portal vein flow volume, and ejection fraction (all p<0.0001*). In Group M30, significant reductions or increases were observed in systolic and diastolic blood pressure, mean arterial pressure, heart rate, serum sodium, urinary volume, urinary sodium, and portal vein flow volume (all p<0.0001*), indicating treatment efficacy. However, creatinine clearance showed a less robust effect (p=0.0382), while other parameters remained unchanged. [Table 3] The analysis of three groups revealed significant differences in their response to treatment across various parameters. Notably, parameters such as ΔMAP, ΔNa, ΔUrinary Na, Δ24 h urinary volume, ΔPV flow volume, and creatinine clearance showed substantial changes across all groups (p<0.0001*). Specifically, Group M2 exhibited the highest ΔNa value (-2.95 ± 1.67) and the lowest Δ24 h urinary volume (-65.00 ± 0.92), indicating a pronounced decrease in sodium levels and urinary volume compared to the other groups. Conversely, Group M30 displayed the highest ΔUrinary Na value (4.60 ± 2.40) and ΔPV flow volume (35.00 ± 1.83), indicating an increase in urinary sodium and portal vein flow volume post-treatment. Additionally, Group A showed the highest ΔBody weight value (-2.10 ± 2.67), indicating a slight decrease in body weight. Creatinine clearance showed significant improvements in all groups, with Group M30 exhibiting the highest value (1.00 ± 1.89), followed by Group A (-13.50 ± 2.44) and Group M2 (-9.00 ± 2.59) (p<0.0001*). Notably, ΔSerum creatinine, Rt RA RI, Lt RA RI, and ΔMELD did not show significant differences among the groups (p>0.05). These findings underscore the varied responses to treatment across different parameters and groups, highlighting the complexity of therapeutic outcomes in cardiovascular and renal health. [Table 4]

DISCUSSION

According to our research, hyponatremia or renal failure are frequently seen by cirrhotic patients with tight ascites having large-volume paracentesis without intravenous albumin. [14] Studies reveal that compared to other plasma expanders, human albumin infusion (6–8 g/L of ascites evacuated) is more efficient in preventing paracentesis-induced circulatory dysfunction (PICD). [15,16] However, due to its cost, our practice has often used alternatives like limiting taps to under 5 liters, using cheaper plasma expanders, or smaller doses of albumin. Recently, vasoconstrictors like vasopressin, terlipressin, and midodrine have been explored as alternatives, but results vary due to small sample sizes, restricting their use to clinical trials. [9,17] The unclear effectiveness of albumin versus vasoconstrictors prompted this trial. The gastrointestinal tract absorbs midodrine, an α-adrenergic agonist, which is then converted by the liver into desglymidodrine, the active form. Midodrine, which is approved for treating symptomatic orthostatic hypotension, has produced conflicting findings in research on problems connected to cirrhosis that impact renal function and systemic and renal hemodynamics. Midodrine increases systemic and splanchnic blood pressure via increasing renal perfusion and effective circulating blood volume. For refractory ascites, midodrine is advised by the American Association for the Study of Liver Diseases. [18,19]

In this investigation, three groups of thirty patients each were randomly assigned. Following LVP, Group A underwent an albumin infusion. For seven days after paracentesis, Group M2 received oral midodrine 12.5 mg every eight hours. Recognizing that previous research suggested the 2-day midodrine regimen was less effective than albumin for preventing circulatory dysfunction—likely due to insufficient dose and duration [9] Group M30 was given the same midodrine dosage for an extended period of 30 days. Follow-up assessments were conducted on day 6 and day 30.

No group in this research saw substantial changes in MAP by day 6. Group A (-4.00 ± 2.68) and Group M30 (-4.50 ± 1.65) showed notable reductions in MAP by day 30 in contrast to Group M2 (1.00 ± 1.53). This shows that increased vasodilation and generally decreased reactivity to vasoconstrictors in cirrhosis may be the cause of midodrine's lack of meaningful effect on MAP. Yosry A et al. [11] observed comparable outcomes, with MAP significantly decreasing in the albumin group (−3.91 ± 7.10) and midodrine 30 group (−4.28 ± 9.56) in contrast to an increase in the midodrine 2 group (0.87 ± 6.67). Adding midodrine to conventional medical therapy (SMT) elevated mean MAP by 2.56 mmHg compared to SMT alone (MD, 3.95 mmHg; 95% CI, 1.53-6.36; p=0.001), according to earlier research like that conducted by Hanafy A et al. [20] and others. On the other hand, midodrine did not significantly alter MAP in comparison to albumin (MD -0.40, 95% CI -2.37 to 1.57; n=164; I2=0%). [21,22] Hamdy H et al. [23] found that there was no significant baseline MAP difference between the albumin and midodrine groups (P=0.238). However, on day 6, there were substantial MAP changes (P<0.001) with albumin (81.33 ± 8.05 to 71.36 ± 7.8 mmHg) and midodrine (78.99 ± 5.52 to 71.93 ± 5.8 mmHg). When midodrine was used in non-azotemic individuals with ascites, there were notable decreases in plasma renin and aldosterone along with conflicting effects for MAP and urine salt excretion. [13] Aboelnasr E et al. [24] discovered that toward the conclusion of the trial, midodrine patients had higher systolic and diastolic blood pressure than controls (P<0.001).

Serum creatinine levels showed no statistically significant variations with respect to renal function (p=0.8808). Nonetheless, there were notable variations (p<0.0001*) in creatinine clearance amongst the groups under investigation. Renal artery resistive indices were similarly affected by this, however not all groups showed a statistically significant trend. Yosry A et al. [11] revealed comparable results, showing no discernible variation in the groups' serum creatinine or creatinine clearance. In both midodrine groups, they observed a considerable or progressive decline in resistive indices, whereas the albumin group showed a minor but noteworthy rise. Systemic and splanchnic blood pressure are raised by α1-agonist midodrine hydrochloride, which increases effective circulating blood volume and

renal perfusion. [18] The lack of a substantial drop in urine volume 30 days after paracentesis in all groups (p<0.0001*) is consistent with these results, indicating similar long-term effectiveness in avoiding hyponatremia or renal impairment. Similarly, Aboelnasr E et al. [24] discovered that there were no appreciable variations in serum creatinine (p=0.472) or sodium (p=0.992) between the midodrine and control groups. Appenrodt B et al. [9] and Hamdy H et al. [23] found that there were no appreciable variations in mean arterial BP, serum creatinine, or serum salt levels between the albumin and midodrine groups. They did find that the albumin group did not have any significant hyponatremia, but the midodrine group saw a large rise in serum creatinine and a very significant fall in serum sodium following therapy. In our investigation, there was no significant difference in the incidence of hyponatremia among the three groups over the study period, despite the fact that the albumin group's serum sodium considerably declined on days 7 and 30. Sola E et al. [25] compared midodrine to a placebo and found that the drug caused renal impairment, hepatic encephalopathy, gastrointestinal bleeding, hyponatremia, and sepsis. Meanwhile, Singh V et al. [10] observed a significant drop in serum sodium post-LVP in both the midodrine and albumin groups, but no hyponatremia development. Interestingly, at 7 and 30 days, there was a substantial increase in urine sodium excretion when midodrine was given for a longer period of time. Each group had a different change in urine sodium excretion; Group M30 had the largest rise [4.60 ± 2.40], while Group A and Group M2 had the lowest increases [1.10 ± 0.87] and [-0.50 ± 1.48]. A suppressed renin-angiotensin-aldosterone system (RAAS), improved renal perfusion, and avoidance of paracentesis-induced circulatory dysfunction (PICD) are the reasons for this increase in sodium excretion in cirrhotic patients treated with midodrine. [21] Similarly, Aboelnasr E et al. [24] also reported a significant increase in urinary sodium levels in the midodrine group compared to the control group. Correspondingly, Singh V et al. [26] discovered that, although this effect decreased after six months, midodrine considerably increased urine sodium excretion after one and three months of medication. Renal plasma flow, glomerular filtration rate, and urinary sodium excretion all increased during a 20-day course of midodrine and octreotide therapy, according to findings by Angeli P et al. [27]. Furthermore, despite midodrine considerably increasing urine sodium excretion, Yosry A et al. [11] observed no discernible variation in the change in urinary sodium across the groups.

In this investigation, the midodrine 30-day group had a considerably greater baseline portal flow volume than the other two groups (p=0.0003*). At days 7 and 30, after LVP, there were notable increases in portal vein flow volume in the albumin and midodrine 2-day groups, indicating better portal hemodynamics. On the other hand, portal vein flow was significantly reduced in the 30-day midodrine group. Similar findings were reported by Yosry A et al. [11], They noticed that the PVF of the albumin and midodrine 2 groups had grown, whereas the midodrine 30 group showed a substantial drop at days 7 and 30. While midodrine may initially improve portal circulation, chronic usage may cause direct vasoconstriction. This rise in the albumin and midodrine 2 groups may be the result of lower baseline portal hemodynamics in the midodrine 30-day group

CONCLUSION

In conclusion, this study highlights the complex interplay between different treatments for cirrhotic patients with tense ascites undergoing large-volume paracentesis. Albumin infusion and midodrine showed varied effects on parameters such as MAP, renal function, urinary sodium excretion, and portal vein flow volume. While albumin and short-term midodrine increased portal haemodynamics and decreased urinary sodium excretion, long-term midodrine use presented a decrease in portal vein flow, indicating potential vasoconstriction effects. Both treatments showed comparable efficacy in preventing renal impairment and hyponatremia. These findings suggest that while albumin remains effective in managing PICD, midodrine could be a viable alternative, although its long-term effects require cautious consideration. Further research is necessary to optimize treatment protocols and improve patient outcomes in this setting.

Limitation

The study's small sample size and single-center design may restrict the broader applicability of the findings.

Recommendation

Future research should prioritize multi-center studies with larger sample sizes to validate results and provide deeper insights into the efficacy of prolonged midodrine use in cirrhotic patients with refractory ascites.

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Tables And Figures

Table 1. Participant baseline characteristics across the three treatment groups.

Characteristic		Group A (n=30)	Group M2 (n=30)	Group M30 (n=30)	P value
Age (years)		49.20 ± 10.50	50.90 ± 12.00	51.30 ± 8.10	F=0.3446 p=0.7094
GENDER	**Male**	22	21	23	X=0.3409 p=0.8433
	Female	8	9	7	
BMI		27.64 ±2.74	28.53 ±2.42	27.86 ±2.84	F=0.9025 p=0.4093
Etiology of liver cirrhosis	**HCV**	29	28	29	X=0.5233 p=0.7698
	HBV	1	2	1	
	HCV+HBV	0	0	0	
Child–Pugh classification	**B**	3/27	5/25	8/22	X=2.889 p=0.2359
	C				
MAP (N: 70–105 mmHg)		85.00 ± 4.50	81.00 ± 5.40a	81.50 ± 4.50a	F=6.137 **p=0.0032***
Diuretics use		24 (80)	25 (83)	27 (90)	X=0.2272 p=0.8926
History of previous tapping		13 (43)	11 (37)	12 (40)	
Volume of ascites removed (l)		5.70 ± 0.85	5.90 ± 0.95	6.15 ± 0.85	F=1.949 p=0.1486
Na (mEq/l)		131.00 ± 3.10	132.70 ± 3.35	132.30 ± 3.50	F=2.149 p=0.1227
Creatinine (mg/dl)		1.25 ± 0.18	1.23 ± 0.23	1.25 ± 0.21	F=0.09274 p=0.9115
Urinary Na [n (%)] (mEq/l)		28.00 ± 11.30	27.00 ± 8.70	24.00 ± 6.30	F=1.604 p=0.2069
24 Urinary volume (l)		1100 ± 220.00	1030 ± 185.00	1120 ± 175.00	F=1.775 p=0.1756
PV flow volume (ml/min)		1580 ± 315	1560 ± 260	1820 ± 200	F=9.109 **p=0.0003***
Right renal artery resistive index		0.69 ± 0.04	0.69 ± 0.03	0.70 ± 0.04	F=0.7317 p=0.4840
Left renal artery resistive index		0.69 ± 0.03	0.70 ± 0.03	0.69 ± 0.03	F=1.111 p=0.3338
Ejection fraction		64.00 ± 6.20	64.50 ± 6.50	66.00 ± 7.50	F=0.7120 p=0.4935

Table 2. Comparative analysis of clinical parameters before and after treatment at six days among three groups.

At 6 day	Group A (n=30)			Group M2 (n=30)			Group M30		
	Before-treatment	**After-treatment**	**P value**	**Before-treatment**	**After-treatment**	**P value**	**Before-treatment**	**After-treatment**	**P value**
Systolic BP (mmHg)	112±6.22	112.8±6.37	t=0.4922 p=0.6245	109.4±7.42	112.8±5.67	t=1.994 p=0.0508	113.8±4.68	108.8±7.33	t=3.149 **p=0.0026***
Diastolic BP (mmHg)	72.8±4.64	70±4.89	t=2.275 **p=0.0266***	66.8±5.24	68.4±5.52	t=1.151 p=0.2543	65.2±5.44	64.8±3.99	t=0.3248 p=0.7465
MAP (mmHg)	85.87±4.51	84.27±4.82	t=1.328 p=0.1895	81±5.39	83.2±5.16	t=1.615 p=0.1118	81.39±4.54	79.47±4.32	t=1.678 p=0.0987

Heart rate (bpm)	88.16 ±3.81	82.44 ±4.66	t=5.205 **p<0.0001***	87.28 ±7.29	82.44 ±4.52	t=3.091 **p=0.0031***	85.2± 4.67	81.44 ±6.38	t=2.605 **p=0.01166***
Serum Na (mEq/L)	131.88±3.16	134.24±2.87	t=3.028 **p=0.0037***	133.68±3.44	132.08±2.76	t=1.987 p=0.0516	133.24±3.59	132.56±3.59	t=0.7336 p=0.4661
PVF flow volume (ml/min)	1493.08±373.7	1793.16±241.2	t=3.695 **p=0.0005***	1557.92±259.64	1956.40±301.07	t=5.490 **p<0.0001***	1828.23±198.77	1711.05±215.46	t=2.189 **p=0.0326***
Urinary Na (mEq/L)	26.74	27.37 ± 3.26	t=0.8699 p=0.3879	22.85 ± 3.57	27.57 ± 2.69	t=5.784 **p<0.0001***	20.75 ± 2.82	29.52 ± 1.28	t=15.51 **p<0.0001***
Serum creatinine (mg/dl)	1.25± 0.18	1.49± 0.33	t=3.497 **p=0.0009***	1.23± 0.23	1.36± 0.33	t=1.770 p=0.0819	1.25± 0.20	1.25 ±0.29	t=0.000 p>0.9999
Creatinine clearance (ml/min)	79.13 ±23.14	62.21 ±23.16	t=2.831 **p=0.0064***	80.45 ±21.87	69.73 ±20.86	t=1.943 p=0.0569	79.83 ±15.89	78.03 ±21.03	t=0.3740 p=0.7097
Right RA RI	0.68± 0.04	0.69± 0.03	t=1.095 p=0.2778	0.69± 0.03	0.69± 0.02	t=0.000 p>0.9999	0.70± 0.04	0.69 ±0.04	t=0.9682 p=0.3369
Left RA RI	0.69± 0.03	0.69± 0.04	t=0.000 p>0.999	0.70± 0.03	0.69± 0.03	t=1.291 p=0.2018	0.69± 0.03	0.69 ±0.03	t=0.000 p>0.9999
EF (%)	64.04 ±6.25	67.2± 4.74	t=2.206 **p=0.0313***	64.48 ±6.55	67.32 ±5.05	t=1.881 p=0.0650	66.92 ±7.58	65.72 ±6.99	t=0.6374 p=0.5263

Table 3. Comparative analysis of clinical parameters before and after treatment at thirty days among three groups.

At 30 days	Group A (n=30)			Group M2 (n=30)			Group M30 (n=30)		
	Before-treatment	**After-treatment**	**P value**	**Before-treatment**	**After-treatment**	**P value**	**Before-treatment**	**After-treatment**	**P value**
Systolic BP (mmHg)	110.09 ± 4.84	112.22 ± 2.51	t=2.140 **p=0.0366***	108.4 ± 1.24	109.2 ± 3.85	t=1.083 p=0.2831	113.04 ± 0.88	104.26 ± 4.37	t=10.79 **p<0.0001***
Diastolic BP (mmHg)	71.74 ± 4.17	68.3 ± 0.60	t=4.472 **p<0.0001***	65.8 ± 2.87	66.4 ± 4.77	t=0.5903 p=0.573	64.56 ± 1.59	63.04 ± 1.67	t=3.611 **p=0.0006***
MAP (mmHg)	85.85 ± 4.30	81.94 ± 3.73	t=3.762 **p=0.0004***	80.55 ± 0.96	80.87 ± 1.96	t=0.8031 p=0.4252	80.62 ± 2.28	77.95 ± 3.69	t=3.372 **p<0.0001***
Heart rate (bpm)	87.13 ± 1.44	84.74 ± 3.13	t=3.799 **p<0.0001***	86.28 ± 2.73	81.92 ± 2.21	t=6.799 **p<0.0001***	84.4 ± 2.24	80.69 ± 2.06	t=6.677 **p<0.0001***
Serum Na (mEq/L)	132.64 ± 2.64	129.76 ± 2.17	t=4.616 **p<0.0001***	133.53 ± 0.60	130.55 ± 3.70	t=4.355 **p<0.0001***	132.68 ± 0.99	129.35 ± 2.53	t=6.713 **p<0.0001***
Urinary Volume (mEq/L)	1090.73 ± 2.47	1165.86 ± 2.39	t=119.7 **p<0.0001***	1035.65 ± 0.66	973.56 ± 3.05	t=109.0 **p<0.0001***	1125.65 ± 2.54	1184.45 ± 2.88	t=83.87 **p<0.0001***
Urinary Na (mEq/L)	27.53 ± 2.52	28.95 ± 3.35	t=1.855 p=0.0686	23.83 ± 4.35	29.15 ± 2.58	t=5.761 **p<0.0001***	21.67 ± 2.50	30.43 ± 1.49	t=16.49 **p<0.0001***
Creatinine (mg/dl)	1.54 ± 4.85	1.33 ± 0.63	t=0.2352 p=0.8150	1.28 ± 0.64	1.38	t=0.4001 p=0.6905	1.25 ± 4.63	1.3 ± 3.63	t=0.04655 p=0.9630
Creatinine clearanc	78.26 ± 3.65	68.37 ± 4.29	t=9.617 **p<0.0001***	81.53 ± 0.68	70.54 ± 3.32	t=17.76 **p<0.0001***	80.67 ± 3.46	82.57 ± 3.48	t=2.121 **p=0.0382***
PVF flow volume (ml/min)	1483.08 ± 2.88	1585.15 ± 2.97	t=135.1 **p<0.0001***	1537.92 ± 1.49	1704.93	t=543.9 **p<0.0001***	1814.77 ± 3.02	1743.48 ± 1.03	t=122.4 **p<0.0001***
Right RA RI	0.67 ± 0.03	0.68 ± 0.07	t=0.7192 p=0.4749	0.68 ± 0.03	0.68 ± 0.02	t=0.000 p>0.9999	0.67 ± 0.08	0.66 ± 0.54	t=0.1003 p=0.9204
Left RA RI	0.68 ± 0.07	0.69 ± 0.03	t=0.7192 p=0.4749	0.69 ± 0.01	0.68 ± 0.09	t=0.6049 p=0.5476	0.68 ± 0.04	0.67 ± 0.21	t=0.2562 p=0.7987
EF (%)	64.74 ± 0.95	69.54 ± 3.52	t=7.211 **p<0.0001***	65.62 ± 2.17	69.61 ± 4.84	t=4.120 **p=0.0001***	66.79 ± 2.90	63.96 ± 2.79	t=3.852 **p=0.0003***

Table 4. Comparative analysis of treatment effects on cardiovascular and renal parameters among three group.

Parameter	Group A (n=30)	Group M2 (n=30)	Group M30 (n=30)	P value
ΔBody weight	-2.10 ± 2.67	-2.30 ± 1.76	-2.15 ± 2.11	F=0.06642 p=0.9358
ΔMAP	-4.00 ± 2.68	1.00 ± 1.53	-4.50 ± 1.65	F=67.98 **p<0.0001***
ΔNa	-1.20 ± 2.33	-2.95 ± 1.67	-0.65 ± 2.50	F=8.973 **p=0.0003***
ΔUrinary Na	1.10 ± 0.87	-0.50 ± 1.48	4.60 ± 2.40	F=70.32 **p<0.0001***
Δ24 h urinary volume	20.00 ± 2.75	-65.00 ± 0.92	55.00 ± 2.46	F=23702 **p<0.0001***
ΔPV flow volume	390.00 ± 2.67	380.00 ± 2.89	35.00 ± 1.83	F=195288 **p<0.0001***
ΔSerum creatinine	0.35 ± 1.57	0.18 ± 2.14	0.10 ± 2.12	F=0.1271 p=0.8808
Creatinine clearance	-13.50 ± 2.44	-9.00 ± 2.59	1.00 ± 1.89	F=305.4 **p<0.0001***
Rt RA RI	0.03 ± 0.78	-0.01 ± 2.19	-0.01 ± 1.03	F=0.007424 p=0.9926
Lt RA RI	0.02 ± 0.69	-0.01 ± 1.37	-0.01 ± 0.98	F=0.008149 p=0.9919
ΔMELD	-0.02 ± 0.92	1.35 ± 1.80	1.50 ± 2.53	F=6.021 **p=0.0036***

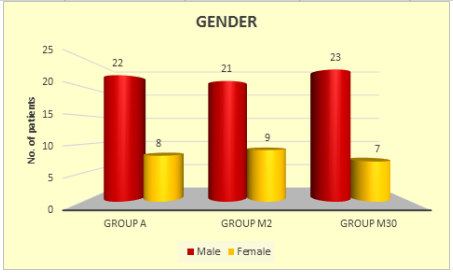

Figure 1. Gender of the enrolled patients among three groups.

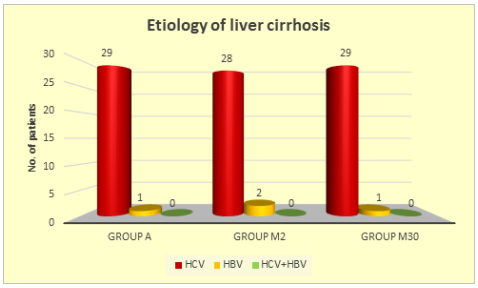

Figure 2. Etiology of the liver cirrhosis among the enrolled patients in three groups.

Figure 3. Comparative analysis of treatment effects on cardiovascular and renal parameters among three group.

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