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Original Article

Prescribing Pattern and Effect of Diuretics in the Management of Ascites: A Comprehensive Study in a Tertiary Care Hospital

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ABSTRACT

Background: Ascites is a medical disorder characterized by fluid accumulation in the peritoneal cavity. Diuretics have been essential in the treatment of ascites, helping to reduce fluid retention and relieve related symptoms. The purpose of this research is to provide a thorough examination of the prescribing trends for diuretics and their effectiveness in managing ascites. Three separate groups of patients will be included in the study: patients who are given furosemide alone, patients who are given spironolactone alone and patients who are given both diuretics together. By using this method, we desire to learn more about the relative merits and potential synergistic effects of various diuretic regimens for the treatment of ascites. **Materials and Methods:** Patients diagnosed with ascites and prescribed diuretics will be identified using diagnostic codes and medication records. Data on prescribing patterns, including types of diuretics, dosages and duration of therapy, will be extracted. Efficacy between the groups was compared by the electrolyte imbalance, weight reduction and urine output-input ratio data. **Results:** 100 liver cirrhosis patients were recruited for this study as per the inclusion-exclusion criteria. Based on the severity of ascites, three different diuretic patterns were prescribed such as monotherapy with Spironolactone (16%) and Furosemide (10%) as well as combination therapy (74%). The study reveals that significant weight reduction and increase in urine output-input ratio was found in the combination group when compared to monotherapy groups. Furthermore, the incidence of electrolyte abnormalities, hyponatremia and hypokalemia was high in the Furosemide group and hyperkalemia was high in the Spironolactone group. **Conclusion:** Management with combination was found to be as economical, safe and effective as Spironolactone monotherapy when compared to Furosemide monotherapy.

Keywords: Diuretics, Ascites, Furosemide, Spironolactone, Prescribing pattern.

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INTRODUCTION

Ascites is the abnormal accumulation of fluid in the abdominal cavity. It is often a complication of cirrhosis, with approximately 50% of patients with compensated cirrhosis developing ascites over time.[1] Cirrhosis is the most common cause of ascites, representing 85% of all cases of ascites. In patients with cirrhosis, ascites due to Portal Hypertension (PHT) are primarily related to an inability to excrete adequate amounts of sodium into urine, leading to a positive sodium balance.[2] Ascites is the most common complication of cirrhosis, as approximately 50% of patients with "compensated" cirrhosis develop ascites during 10 years of follow-up.[3] The impairment in the renal ability to excrete sodium is considered the earliest manifestation of renal dysfunction in cirrhosis as shown by reduced natriuretic response to acute administration of sodium chloride.[4] Diuretics have been the mainstay of the treatment of ascites. Renal sodium retention in the setting of liver cirrhosis and ascites is due to increased proximal and distal tubular reabsorption of sodium.[5] Usually, two broad classes of diuretics are used for the management of ascites namely, Spironolactone, an aldosterone antagonist at a starting dose of 50 to 100 mg/day and Furosemide, a loop diuretic a low dose of 20 to 40 mg/day.[6] Dietary sodium restriction and a dual diuretic regimen with spironolactone and furosemide are effective in more than 90% of patients in achieving a reduction in the volume of ascites to acceptable levels.[7] Comparison of both single and combination diuretic therapy based on safety as well as effectiveness would be of practical advantage in the management of these common hepatic complications and help to reduce the risk of remission of disease as well as re-hospitalization. This study aims to evaluate the use of different diuretics and effective diuretic regimens in the management of hepatic diseases.

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MATERIALS AND METHODS

A Prospective Observational Study was carried out in the Department of Gastroenterology, PSG Hospitals, Coimbatore, with the subjects having Liver cirrhosis who were on diuretic therapy. A total patient of 100 was recruited as per the sample size calculation for the study and enrolled patients over six months. The approval of the study, with proposal number 14/040 was obtained from Institutional Human Ethics Committee. The data sources were the case files and patient interviews. The study includes people of age above 18 years with hepatic disease treated with diuretics excluding pregnancy, lactating and oliguric renal failure patients. Sociodemographic data such as age and weight along with medical and medication history including co-morbidities, past medications, lab values, diagnosis and current medications were collected by using a data collection form. After obtaining informed consent, patient demographics, social habits, diagnosis, past medical and medication history, lab reports and current medication reports were collected from the case files. Objective data of the patient such as weight changes and urine output-input ratio were also recorded from the case file during the hospital stay using a data collection form. After collecting all these data, patient diagnosis and treatment with diuretics were assessed and they were enrolled into different treatment groups. Those are, group 1 (patients taking Spironolactone), group 2 (patients taking Furosemide) and group 3 (patients taking Spironolactone and Furosemide). Significance between the three groups was analyzed by one-way ANOVA followed by Dunnet multiple comparison test values less than 0.5 were fixed as the criterion for the statistical significance shown in Figure 1.

RESULTS

Out of 120 patients with liver cirrhosis who were screened, 100 patients with ascites were included in the study. The patient's medical record and prescription pattern were analyzed during the study. The patients in the age group between 18 to 40 were 16%, 41 and 60 were 59%, 61-80 were 24% and those above 80 were 1%, respectively. The male population of the study was 88% and the female population was 12%. The etiological factors of patients with ascites include alcohol (71%), virus (8%) and cryptogenic (21%). The physical findings were oedema (48%), hepatomegaly (20%), splenomegaly (56%) and jaundice (48%). Hypertension was the predominant co-morbidity (17%), followed by diabetes (10%), anaemia (12%), asthma (2%), infection (2%) and a few multiple conditions like diabetes with hypertension (4%) and hypertension with anaemia (5%). The grading of patients is based on the severity of ascites, which consists of grades I (40%), II (57%) and III (3%). The complications among study participants were portal hypertension (60%), esophageal varices (53%), encephalopathy (40%) and SBP (20%). The demographics of the patients were represented in Table 1.

Based on the severity of the ascites, spironolactone (14%, furosemide (5% and combined drugs (20%) were given for grade I. In grade II, spironolactone had 1%, furosemide had 5% and a combination of 52% was treated. 3% of the combination was given to grade III. Entirely, 16% received spironolactone, 10% received furosemide and 74% received a combination of spironolactone and furosemide. The prescribing pattern of a diuretic regimen in managing ascites is represented in (Figure 2).

The efficacy of the diuretics was assessed using electrolyte balance, weight reduction and urine input-output ratio. The electrolyte levels of sodium, potassium, bicarbonate and chloride in all three treatment groups were monitored before and after the drug treatment. The sodium level before administering spironolactone was 138±4.1 and after, it became 138±4.7. Similarly, for furosemide, it was 135±3.7 to 132.8±6. In the combination group, it was 133.5±3.7 to 132.8±4.6. The potassium level before the spironolactone treatment was 3.6±4.7 and after treatment, it increased to 3.7±0.4. With furosemide, it was 4.2±0.64 and 4.2±0.62. With the combination group, it was 4.1±0.7 and after, it became 4.05±0.5. The bicarbonate was not significantly (p=0.08) changed in all three groups: spironolactone (22±2 to 22.2±2), furosemide (22.1±4.7 to 22.05±4.07) and the combination group (21.1±3.3 to 21. 7±2.6). There was a slight increase in chloride after the treatment in all groups, i.e., 100.6±5 to 101±4, 98.6±3 to 99.3±2.5 and 99.4±4.2 to 100.3±3.6, respectively. A statistically significant difference was not seen while comparing the electrolyte levels between the groups. All the values given for the electrolytes are represented as Mean±SD in Table 2.

30% and 12.5% of the patient's sodium levels deviated to hypo condition were 4.76±2.31 and 2.58±0.48 in the spironolactone and furosemide respectively. In combination, 18.9% had normal to hypo value of 6.37±1.7 and had hypernatremia of 7.46±1.95,

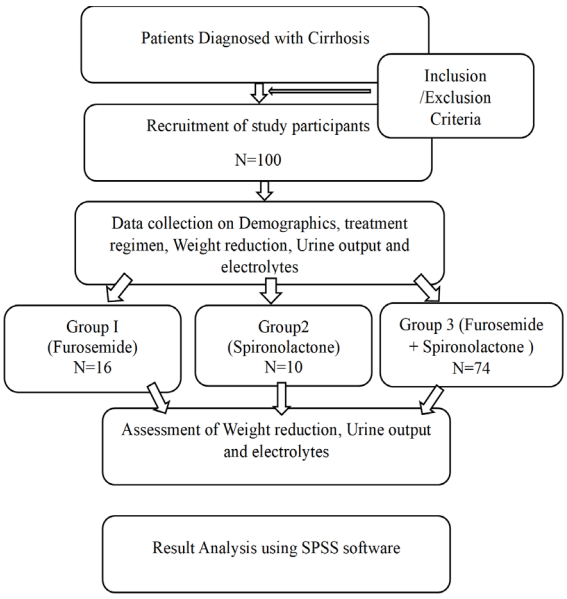

Figure 1: Flowchart for methodology.

Table 1: Demographics of the study participants.

Demographics	*n*=100(%)	Treatment Groups			*p* Value
		Furosemide *n*=16 (%)	Spironolactone *n*=10 (%)	Combination *n*=74 (%)	
Age 18-40 41-60 61-80 >80	16(16) 59(59) 24(24) 1(1)	4(25) 6(37.5) 6(37.5) -	3(30) 3(30) 4(40) -	9(12.16) 50(67.56) 14(18.91) 1(1.3)	0.21
Gender Male Female	88(88) 12(12)	12(75) 4(25)	5(50) 5(50)	71(95.9) 3(4.1)	0.33
Causes Alcoholic Viral Cryptogenic	71(71) 8(8) 21(21)	7(43.75) 2(12.5) 7(43.75)	5(50) 2(20) 3(30)	59(79.73) 4(5.4) 11(14.86)	0.23
Comorbidities Diabetes Hypertension Anemia Asthma Infection	14(10) 21(17) 22(12) 2(2) 7(2)	2(12.5) 4(25) 3(18.75) 2(12.5) 1(6.25)	2(20) 3(30) 3(30) - 2(20)	10(13.51) 14(18.91) 6(8.11) - 4(5.4)	0.44
Grading Grade I (Mild) Grade II (Moderate) Grade III (Severe)	39(39) 58(58) 3(3)	14(87.5) 2(12.5) -	5(50) 5(50) -	20(27.03) 51(68.92) 3(4.1)	0.03*
Complications Portal hypertension Oesophageal varices Encephalopathy SBP	60(60) 53(53) 40(40) 20(20)	15(25) 14(26.42) 5(12.5) 2(10)	10(16.67) 12(22.64) 9(22.5) 4(20)	35(58.33) 27(50.94) 26(65) 14(70)	0.12

* indicates significant *p*-value<0.05; SBP: Spontaneous Bacterial Peritonitis.

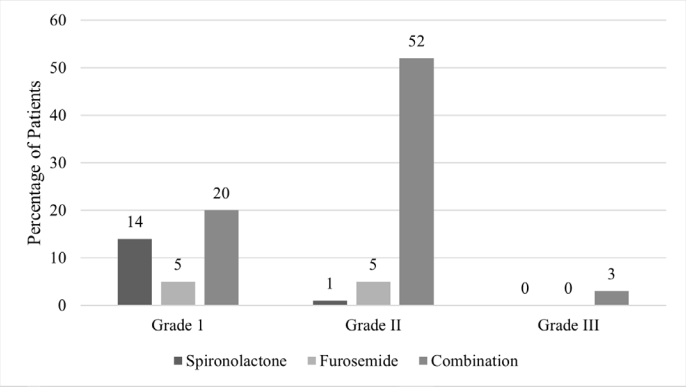

Figure 2: Prescribing pattern of diuretic regimens in the management of ascites.

which is statistically more significant than monotherapy. 20% of patients had hypokalemia with 16.77±6.5 in furosemide and 6.75% in the combination group with a deviation of 19.39±3.25. 18% of patients had hyperkaliemia in Spironolactone with a value of 2.99±6.31 and the combination had a deviation of 18.95±8.83 among 4%. Hyperkaliemia and hypokalemia are statistically more significant in combination than in furosemide therapy, as well as in furosemide than in spironolactone therapy. No statistical difference was observed between spironolactone and combination therapy. Table 3 describes the deviation of serum sodium and potassium concentration from normal levels. Weight and Urine Output-Input Ratio Changes of three treatment groups among sodium, potassium, bicarbonates and chlorides show optimal differences in the combination group compared to the other two groups and they are represented in Table 4.

Table 2: Weight and urine output/input ratio changes of three treatment groups.

Treatment Groups	Weight Reduction			Urine Output/ Input Ratio		
	Before (Mean±SD)	After (Mean±SD)	Mean difference	Before (Mean±SD)	After (Mean±SD)	Mean difference
Furosemide	74.04±3.2	72.22±3.1	1.8±0.66	0.71±0.53	1.01±0.23	0.30±0.20
Spironolactone	71.02±2.28	69.42±2.4	1.6±0.65	0.86±0.15	1.20±0.34	0.34±0.31
Combination	69.88 ± 2	67.70±2.38	2.7±0.7	0.59±0.22	1.09±0.51	0.50±0.21

* indicates significant *p*-value<0.05

Table 3: Deviation of serum sodium and potassium concentration from normal level.

Electrolytes	Spironolactone *n*=16 (Mean+SD)		Furosemide *n*=10 (Mean+SD)		Combination *n*=74 (Mean+SD)	
	Before	After	Before	After	Before	After
Sodium	138±4.1	138±4.7	135.3±3.7	132.8±6	133.5±3.7	132.8±4.6
Potassium	3.6±4.7	3.7±0.4	4.2±0.64	4.2±0.62	4.1±0.7	4.05±0.5
Bicarbonates	22±2	22.2±2	2.1±4.7	22.05±4.7	21.1±3.3	21.7±2.6
Chloride	100.6±5	101±4	98.6±3	99.3±2.5	99.4±4.2	100.3±3.6

* indicates significant *p*-value<0.05

Table 4: Electrolytes Changes of three treatment groups.

Treatment Groups	Electrolytes	Hypo	%	Hyper	%
Furosemide	Sodium	4.76±2.31	30	-	
	Potassium	16.77±6.50*	20	-	
Spironolactone	Sodium	2.58±0.48	12.5	-	
	Potassium	-		12.99±6.31	18
Combination	Sodium	6.37±1.7*	18.9	7.46±1.95*	2
	Potassium	19.39±3.25*	6.75	18.95±8.83*	4

* indicates significant *p*-value<0.05

The most frequent cirrhosis complication is ascites, which is associated with poor quality of life, a high chance of developing other cirrhosis complications, increased morbidity and mortality from surgical procedures and a high risk of renal failure.

Ascites have traditionally been treated with diuretics, which are Spironolactone at a starting dose of 50 to 100 mg/day and Furosemide at a lower dose of 20 to 40 mg/day, either mono or combination therapy. In this study, the main leading cause of cirrhosis was alcoholism, which was followed by hepatitis, which was similar to previous studies in which the primary cause of cirrhosis was alcoholism, which accounted for 75% to 80% of all cases (ECU, Center for Health Services Research and Development, 2001). Alcohol consumption increases the mortality rates, especially from Cirrhosis of the liver (leading to last stage cirrhosis-ascites) and other forms of liver disease. The male population with ages above 40 years developed cirrhosis with complications of ascites.

DISCUSSION

The incidence of ascites among chronic liver disease patients was found to be 83%. The prescribing pattern was found to be different in each grade of ascites. The male population was 88% and the female population was 12%, patients between the age group 41-60 were more with 59%. The International Ascites Club reports that diuretic medication was mostly advised for Grade II and III ascites.

In a study led by Michael R. Fogel and his team, they looked at how well diuretics work for ascites, a condition where fluid builds up in the abdomen. They found that the group taking a combination of diuretics had lower sodium levels in their blood compared to those taking just Furosemide. However, the group taking Spironolactone didn't see much change in sodium levels. Also, the Spironolactone group had higher potassium levels compared to the Furosemide group. When comparing the Combination

group to the other two groups, their potassium levels were in the middle. Additionally, both the Spironolactone and combination groups had a small drop in bicarbonate compared to the Furosemide group, but these differences weren't big enough to be significant according to the study.

In line with the results of the randomized study, there was marked hyponatremia in the combination group and severe hyperkalemia in the combination and spironolactone group. K Bind Sachet was administered to 4 out of 5 individuals with hyperkalemia to get their potassium levels back to normal.

In our investigation, we found that hypokalemia was mostly seen in the Combination group, while in the randomized experiment, it was only observed in the Furosemide group. We didn't notice any clear difference in bicarbonate and chloride levels. Six people with low potassium levels were given KCl supplements, which successfully brought their potassium levels back to normal.

In our study, we observed a notable weight loss ($p<0.05$) in the Combination group. While those who received furosemide also experienced some weight loss, the overall reduction in weight across the three therapy groups was similar. Similarly, a similar number of individuals across all groups experienced resolution of their ascites. However, ascites resolved slightly earlier in the Combination group.

Comparing the Combination and Spironolactone groups, the increase in urine output-input ratio was noticeably larger in the Combination group. Prior research has shown that when compared to other therapies, spironolactone medication delayed the onset of diuresis. This was due to the treatment group's inability or unwillingness to lose weight. Diuresis began rather quickly after beginning the combination therapy.

When we compare the effectiveness of diuretics in terms of weight loss and urine output-input ratio, the combination group notably reduced weight and increased urine output-input ratio compared to the other two groups using only monotherapy, Furosemide and Spironolactone. In the Furosemide group, there was a significant prevalence of electrolyte abnormalities such as hyponatremia and hypokalemia, while the Spironolactone group had a high prevalence of hyperkalemia.

CONCLUSION

The incidences of ascites among Chronic liver disease patients were found to be 83%. Grade I ascites were mostly treated with Spironolactone and a Combination regimen, whereas in Grade II and III, only combination regimens were prescribed. When comparing the efficacy of diuretics based on weight reduction and urine output-input ratio, significant weight reduction and increase in urine output-input ratio was found with combination therapy. Thus, it can be concluded that, even though Furosemide is of low cost, it is less effective and electrolyte abnormalities were more and it is often requiring KCl supplementation. Management with Combination was found to be as economic, safe and effective as Spironolactone monotherapy when compared to Furosemide monotherapy.

AUTHOR CONTRIBUTION

All authors reviewed and edited the manuscript and approved the final version of the manuscript. Substantial contributions to the conception: Rama Parthasarathy, Swathy Pradeep, Sobby Annie John, Divakar G; design of the work; writing: Divakar G, analysis of data: Rama Parthasarathy, Divakar G; the acquisition, analysis of data: Rama Parthasarathy, Swathy Pradeep, Sobby Annie John; interpretation of data for the work: Rama Parthasarathy, Divakar G; drafting the work or revising it critically for important intellectual content: Rama Parthasarathy, Divakar G.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

mg: Milligram; **ANOVA:** Analysis of Variance; **SBP:** Spontaneous Bacterial Peritonitis; **SD:** Standard Deviation; **K:** Potassium; **KCl:** Potassium Chloride.

SUMMARY

Ascites, the abnormal accumulation of fluid in the abdomen, is a common complication of cirrhosis. In this study, 100 individuals with liver cirrhosis had their ascites managed with diuretics. When compared to monotherapy, combination therapy demonstrated a substantial decrease in weight and an increase in the urine output-input ratio. Spironolactone, furosemide and combination therapy were also evaluated. In contrast to spironolactone monotherapy, which showed hyperkalemia, furosemide monotherapy showed anomalies in electrolytes. Spironolactone and combination therapy were the primary treatments for Grade I ascites, although combination therapy was more common in Grade II and III cases. The results indicate that combination therapy is a cost-efficient substitute for furosemide monotherapy in the management of ascites related to liver cirrhosis and it is just as safe and efficacious as spironolactone monotherapy.

REFERENCES

1. Ascites. 2022;413-5.

2. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. Ann Intern Med. 1992;117(3):215-20.
3. Ginés P, Quintero E, Arroyo V, Terés J, Bruguera M, Rimola A, *et al.* Compensated cirrhosis: natural history and prognostic factors. Hepatology. 1987;7(1):122-8.
4. Pathophysiology, diagnosis and treatment of ascites in cirrhosis - PubMed [Internet]. [cited 2024 Mar 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/15115971/
5. Management of refractory ascites-PubMed [Internet]. [cited 2024 Mar 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/35676862/
6. Runyon BA. Care of patients with ascites. N Engl J Med. 1994;330(5):337-42.
7. Stanley MM, Ochi S, Lee KK, Nemchausky BA, Greenlee HB, Allen JI, *et al.* Peritoneovenous shunting as compared with medical treatment in patients with alcoholic cirrhosis and massive ascites. Veterans Administration Cooperative Study on Treatment of Alcoholic Cirrhosis with Ascites. N Engl J Med. 1989;321(24):1632-8.

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