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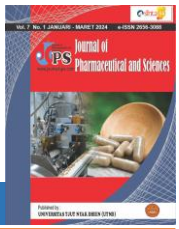

Study of Diuretic in Cirrhosis Hepatic Patients with Ascites Complication at dr Iskak Tulungagung General Hospital

Studi Pemberian Diuretik Pada Pasien Sirosis Hepatik Dengan Komplikasi Asites di RSUD dr. Iskak Tulungagung

Agies Annastasya P.D. [a], Alvina Arum Puspitasari [a]*, Didik Hasmono [a] and Binti Muzayyanah [b]

[a] *Department of pharmacy, Faculty of health sciences, University of Muhammadiyah Malang, East Java, Indonesia*
[b] *dr Iskak Tulungagung General Hospital, East Java, Indonesia.*

Corresponding Authors: alvinaap@umm.ac.id

Abstract

According to the World Health Organization (WHO), cirrhosis is a structural change of the liver from normal to abnormal, characterized by fibrosis. Ascites is the most common complication in liver cirrhosis patients with the primary trigger (75%) is portal hypertension. The treatment focuses on removing the fluid from the peritoneal cavity. This study aim to understanding the pattern of diuretic use as ascites therapy in patients with cirrhosis hepatic. An observational study with a retrospective and descriptive approach using total sampling method in patients diagnosed with cirrhosis and ascites who received diuretics at Dr Iskak Tulungagung general hospital during January-December 2022 were conducted. The tools used in this study include medical records, data collection sheets, clinical data sheets, and laboratory data. Among 62 patients, 16 (26%) received spironolactone monotherapy, 9 (14%) furosemide monotherapy, 21 (34%) combination therapy, and 16 (26%) underwent switching between regimens. Spironolactone, particularly at 100 mg orally once daily, either alone or in combination with furosemide (40 mg intravenously once daily), was the most frequently prescribed diuretic regimen. These findings indicate that the therapeutic approach applied in clinical practice has generally followed the AASLD guideline recommendations.

***Keywords*: Cirrhosis, Ascites, Diuretic, Spironolactone.**

Abstrak

Menurut World Health Organization (WHO), sirosis adalah perubahan struktur hati dari normal menjadi abnormal yang ditandai dengan fibrosis. Asites merupakan komplikasi tersering pada pasien sirosis hati dengan pemicu utama (75%) adalah hipertensi portal. Penanganan difokuskan pada pengeluaran cairan dari rongga perut. Penelitian ini bertujuan untuk mengetahui pola penggunaan diuretik sebagai terapi asites pada pasien sirosis hati. Penelitian ini merupakan penelitian observasional dengan pendekatan retrospektif dan deskriptif menggunakan metode *time limit sampling* pada pasien yang terdiagnosis sirosis dan asites yang mendapatkan diuretik di RSUD dr. Iskak Tulungagung selama bulan Januari-Desember 2022. Instrumen yang digunakan dalam penelitian ini meliputi rekam medis, lembar pengumpulan data, lembar data klinis, dan data laboratorium. Di antara 62 pasien, 16 (26%) menerima monoterapi spironolakton, 9 (14%) monoterapi furosemid, 21 (34%) terapi kombinasi, dan 16 (26%) menjalani pergantian regimen. Spironolakton, terutama dengan dosis 100 mg oral sekali sehari, baik tunggal maupun kombinasi dengan furosemid (40 mg intravena sekali sehari), merupakan regimen diuretik yang paling sering diresepkan. Temuan ini menunjukkan bahwa pendekatan terapeutik yang diterapkan dalam praktik klinis secara umum telah mengikuti rekomendasi pedoman AASLD.

***Kata Kunci*: Sirosis, Asites, Diuretik, Spironolakton.**

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Introduction

The liver is the second-largest organ in the human body, performing crucial functions including energy metabolism, plasma protein synthesis, and metabolic regulation [1]. Cirrhosis hepatic represents a major global health burden, with mortality rates increasing by 47.15% worldwide between 1990 and 2017 [2]. In developed countries, the primary causes include hepatitis B and C, non-alcoholic fatty liver disease, and excessive alcohol consumption [3]. Indonesia faces a particularly high burden, with 7.1% of the population infected with hepatitis B according to Riskesdas 2013 data [4]. Cirrhosis is a chronic condition characterized by damage to normal liver tissue, leading to regenerative nodules surrounded by dense fibrotic material. This distorted architecture impedes portal blood flow, disrupting hepatocyte perfusion and hepatic synthetic functions [3]. Patients may present with compensated or decompensated cirrhosis, with the latter showing complications such as ascites, hepatic encephalopathy, and portal hypertension [5].

Ascites, the accumulation of fluid in the peritoneal cavity, is one of the most common complications of cirrhosis. The pathophysiology involves portal hypertension causing increased intrahepatic resistance and elevated sinusoidal pressure. Combined with decreased oncotic pressure, this leads to excess sodium and fluid being pushed into the lymphatic system. When lymphatic capacity is exceeded, fluid spills into the peritoneal cavity, forming ascites [6]. Current therapeutic approaches for ascites follow established guidelines from the American Association for the Study of Liver Diseases (AASLD). For stage one ascites, treatment involves aldosterone antagonist diuretics such as spironolactone (100 mg once daily) or dietary salt restriction to 2 grams per day. Advanced stages (two and three) require combination therapy with spironolactone and loop diuretics like furosemide (40 mg once daily). Spironolactone dosage can be increased every seven days due to its delayed natriuretic effect, while furosemide can be adjusted every two to three days [7]. For refractory stage three ascites, large volume paracentesis (LVP) with hyper-oncotic human albumin becomes the treatment of choice [8].

Diuretics work by promoting water and electrolyte excretion through the kidneys, increasing urine formation and reducing extracellular fluid volume. Spironolactone, an aldosterone antagonist, increases potassium levels while reducing sodium concentration, making it particularly effective in managing ascites and hypertension [9]. Furosemide, a loop diuretic, provides additional therapeutic benefits in various conditions beyond ascites management [10].

Despite clear therapeutic guidelines, there remains a significant gap in understanding how these evidence-based recommendations are implemented in clinical practice. The adherence to guideline-recommended diuretic therapy patterns, including appropriate dosing, administration routes, and combination strategies, varies considerably across healthcare institutions. This study aims to evaluate the patterns of single and combined diuretic use in patients with liver cirrhosis and ascites complications, specifically examining dosage, route of administration, and frequency of administration to assess compliance with established therapeutic guidelines and identify areas for improvement in clinical practice.

Materials and Methods

This study employed an observational, retrospective descriptive design using medical records of patients diagnosed with liver cirrhosis and ascites who received diuretic therapy at Dr. Iskak General Hospital, Tulungagung, from January to December 2022. A total sampling method was applied, including all patients

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who met the inclusion criteria (complete medical records, diagnosis of cirrhosis with ascites, diuretic use) and excluding those with incomplete data or major comorbidities (e.g., end-stage chronic kidney disease). Data were collected using a structured form covering demographics (age, sex), clinical data (diagnosis, length of stay, outcome), therapy details (diuretic type, dose, route, frequency), and relevant laboratory results (liver function, kidney function, electrolytes). Data collection took place between January and March 2024.

Results and Discussion

From this research, 102 patients with liver cirrhosis were identified at Dr. Iskak General Hospital in Tulungagung Regency from January 1 to December 31, 2022. Out of this population, 62 medical records met the inclusion criteria, and this study did not have any exclusion criteria.

Table 1. Characteristics of Liver Cirrhosis Patients with Ascites at Dr. Iskak General Hospital Tulungagung

Patients Characteristic	n	%
Gender		
Male	40	65
Female	22	35
Total	62	100
Age		
19-44 years	8	13
45-59 years	23	37
>60 years	31	50
Total	62	100
Hospital Length of Stay		
1 - 3 days	8	13
4 - 6 days	27	44
7 - 10 days	17	27
>10 days	10	16
Total	62	100
Patient Condition During Hospital Discharge		
Improved	42	68
Died	20	32
Total	62	100

According to the data obtained, male patients are more frequently afflicted with cirrhosis and ascites (65%) compared to females. Research conducted by Darren Tan and colleagues from 2010 to 2019 showed that the global prevalence of cirrhosis is higher among men than women, with an increase of 12% in men and 9% in women [11]. This is because males are more susceptible to conditions that can lead to cirrhosis hepatic, such as hypertension and diabetes. Males are also more often exposed to agents causing cirrhosis, such as excessive alcohol consumption and hepatitis viruses [4].

Patients aged ≥60 years are most frequently affected by liver cirrhosis with ascites (50%), according to the research findings. A study conducted by Mutiara and colleagues in 2023 showed that the age group 51-60 years had the highest frequency, with a total of 25 patients (45.5%). Another study by Dwi in 2019 aligns with Mutiara's research, showing that the age group 41-60 years had the highest frequency, with a total of 19 patients (51.4%). This is because liver damage takes years to develop into cirrhosis. As age increases, cirrhosis becomes more commonly observed. Viral infections acquired in youth may manifest as cirrhosis many years later. Other factors influencing age-related cirrhosis include decreased immune function, morphological aging, reduced liver function, liver weight, and blood flow in the liver [12].

The length of hospital stays for patients with cirrhosis and ascites commonly falls within the 4-6 days range (44%). The variation in hospital stay among patients is influenced by the severity of the disease and any comorbid conditions. Patients with multiple complications or unstable conditions may require hospitalization

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for up to 20 days. Conversely, patients admitted for only two days might be undergoing check-ups and managing ascitic fluid removal due to previous hospitalizations for ascites. Therefore, the duration of hospital stay varies among patients. At Dr. Iskak General Hospital, 68% of cirrhosis patients experienced improvement in their condition. The quality of life for patients with cirrhosis can be assessed using the Child-Pugh criteria. The more severe the disease, the lower the quality of life score [13]. Patients with compensated cirrhosis may have a better quality of life compared to those with decompensated cirrhosis [6].

Table 2. Diuretic Therapy Use in Patients with Liver Cirrhosis and Ascites

Diuretic Pattern	n	%
Spironolactone Monotherapy	16	26
Furosemide Monotherapy	9	14
Combination therapy (Spironolactone + Furosemide)	21	34
Switching between regimens (either from monotherapy or combination)	16	26
Total	**62**	**100**

In this research, combination therapy (34%) was the most frequently prescribed diuretic use pattern. The combination of spironolactone and furosemide is used when ascites has recurred (grade 2 ascites) or in cases of refractory ascites. This combination typically results in a better response compared to using a single diuretic [8]. Additionally, spironolactone is combined with furosemide to decrease side effects. Furosemide is a potent diuretic that can rapidly remove fluid but does not retain potassium, making its use alone risky for hypokalemia. Therefore, spironolactone, which is potassium-sparing, is necessary to counteract the effects of furosemide [14]. Spironolactone, either alone or in combination with furosemide, was the most frequently prescribed diuretic type. According to research cited by the AASLD in their guidelines, the first episode of ascites responds adequately to spironolactone with minimal side effects [8]. Furosemide is used as the first-line therapy for grade 2 ascites [14].

Table 3. Pattern of Diuretic Monotherapy in Patients with Liver Cirrhosis and Ascites

Pattern	n[1]	%
Spironolactone (1x25 mg) po	7	6
Spironolactone (1x50 mg) po	2	2
Spironolactone (1x100mg) po	45	40
Spironolactone (2x100mg) po	4	3
Furosemide (1x20 mg) iv	9	8
Furosemide (2x20 mg) iv	5	4
Furosemide (3x20 mg) iv	3	3
Furosemide (2x30 mg) iv	1	1
Furosemide (1x40 mg) po	2	2
Furosemide (1x40 mg) iv	20	18
Furosemide (2x40 mg) iv	8	7
Furosemide (3x40 mg) iv	6	5
Total	**112**	**100**

[1]each patient can receive more than one pattern

Therapy for patients with cirrhosis and ascites typically begins with spironolactone at a dose of 100 mg, which can be increased up to 400 mg, while furosemide starts at 40 mg and can be increased up to 160 mg. Dose adjustments are made based on the patient's needs. If ascites is adequately managed with spironolactone at a dose of 100 mg orally once daily and furosemide at a dose of 40 mg intravenously once daily, there is no need to increase the dosage. Instead, the dosage should be reduced to the lowest effective level to maintain minimal or no ascites, in order to minimize the side effects of diuretic use [8].

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Table 4. Pattern of Combination Diuretic Therapy in Patients with Liver Cirrhosis and Ascites

Pattern	n[1]	%
Spironolactone (1x25 mg) po + Furosemide (1x20 mg) iv	1	2
Spironolactone (1x25 mg) po + Furosemide (3x20 mg) iv	1	2
Spironolactone (1x50 mg) po + Furosemide (2x20 mg) iv	1	2
Spironolactone (1x50 mg) po + Furosemide (2x40 mg) iv	1	2
Spironolactone (1x50 mg) po + Furosemide (3x40 mg) iv	1	2
Spironolactone (1x100 mg) po + Furosemide (1x20 mg) iv	8	17
Spironolactone (1x100 mg) po + Furosemide (2x20 mg) iv	3	6
Spironolactone (1x100 mg) po + Furosemide (3x20 mg) iv	1	2
Spironolactone (1x100 mg) po + Furosemide (1x40 mg) iv	17	37
Spironolactone (1x100 mg) po + Furosemide (1x40 mg) iv	2	4
Spironolactone (1x100 mg) po + Furosemide (2x40 mg) iv	4	9
Spironolactone (1x100 mg) po + Furosemide (3x40 mg) iv	1	2
Spironolactone (2x100 mg) po + Furosemide (1x20 mg) iv	1	2
Spironolactone (2x100 mg) po + Furosemide (2x40 mg) iv	3	6
Spironolactone (2x100 mg) po + Furosemide (3x40 mg) iv	1	2
Total	**41**	**100**

[1]not all patient are given combination therapy

The most frequently used combination therapy was spironolactone (100 mg orally once daily) with furosemide (40 mg intravenously once daily), applied in 37% of patients receiving combination therapy. This therapy pattern aligns with the guidelines provided by the AASLD. In addition to this regimen, various other combination therapies are employed. This variability arises because each patient's therapeutic needs are different, necessitating adjustments in therapy. Generally, the lower the dosage administered, the smaller the risk of complications due to the side effects of diuretic use [8].

Conclusions

Based on this study, the use of diuretics for ascites therapy in patients with liver cirrhosis at Dr. Iskak General Hospital predominantly involved spironolactone and furosemide, which are in line with international guideline recommendations. The most common dosing regimens identified were spironolactone 100 mg orally once daily and furosemide 40 mg intravenously once daily, either as monotherapy or in combination. These findings indicate that the therapeutic approach applied in clinical practice has generally followed the AASLD guideline recommendations.

Conflict of Interest

There is no conflict of interest in this research.

Acknowledgment

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