

MONITORING OF EFFECTIVENESS OF SPIRONOLACTONE THERAPY AND ITS COMBINATIONS WITH FUROSEMIDE TO LIVER CIRRHOSIS AND ASCITES IN RSUP H. ADAM MALIK MEDAN

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ABSTRACT

Objectives: Spironolactone and furosemide are diuretics used to treat liver cirrhosis with ascites, but not case studies have been found to distinguish the effects of spironolactone and its combination with furosemide in cases of cirrhosis accompanied by ascites. This study aims to determine the effectiveness of spironolactone therapy and its combination with furosemide to liver cirrhosis patients accompanied ascites.

Methods: This research was done by cross-sectional prospective method. 26 patients staying at RSUP H. Adam Malik Medan For 3 months were divided into 2 groups. The first group of nine patients, age between 39 and 65 years, was given spironolactone. The second group of 17 patients, age between 20 and 81 years, was given spironolactone combined with furosemide. The sample data were analyzed with statistics using Mann-Whitney U-test, SPSS program version 22.

Result: Based on Mann-Whitney U statistic test, the value of p value. Significance (2-tailed) 0.435 for urine Na/K at time, and Asymp. significance value (2-tailed) 0.628 24 h urine sodium examination, based on the value, it was concluded that there was no significant difference between spironolactone with its combination with furosemide. Even though the significant value was 0.628 mEq and 0.435 mEq ($p > 0.05$).

Conclusion: This study showed that the combination of spironolactone with furosemide was better than compared to spironolactone. Moreover, there was no statistically significant difference compared with 24 hours of urine sodium value with a normal value of 78 mEq.

Keywords: Cirrhosis, Ascites, Spironolactone, Its combinations with furosemide.

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INTRODUCTION

Liver cirrhosis is the ultimate pathology of various liver diseases [1]. The term cirrhosis was first introduced by Laennec in 1826. Cirrhosis of the liver comes from the Greek word *scirrhos* or shows the orange or brownish-yellow color of the surface of the liver seen at autopsy. Many forms of liver damage are characterized by fibrosis. Fibrosis is an excessive buildup of extracellular matrix in the liver. The fibrosis response to liver damage is reversible. However, in most patients with liver cirrhosis, the fibrosis process is not reversible [2].

According to the World Health Organization, in 2000, about 170 million suffered from liver cirrhosis. This number accounts for about 3% of the total human population in the world and every year the incidence of new liver cirrhosis increases from 3 to 4 million people. Chronic liver disease and liver cirrhosis can cause about 35,000 deaths year in the United States. Cirrhosis is the ninth leading cause of death in the United States [3,4]. Liver cirrhosis is the most common cause of ascites in the United States, accounting for about 85% of cases [5].

The prevalence rate of liver cirrhosis disease in Indonesia is definitely not known. However, from several reports of the public hospital in Indonesia based on clinical diagnosis, the prevalence of cirrhosis of the liver treated in the ward of the disease generally ranges from 3.6% to 8.4% in Java and Sumatera, while in Sulawesi and Kalimantan below 1%. Overall, the average prevalence of liver cirrhosis was 3.7% of all patients treated in the internal medicine ward or an average of 47.4% of all treated liver disease patients [2].

The major complications of liver cirrhosis include ascites, hepatic encephalopathy, portal hypertension, variceal hemorrhage, and hepatorenal syndrome [6]. Treatment of cirrhosis of the liver and ascites begins with salt diet, salt consumption of 5.2 g or 90 mEq/day. Low-salt diet combined with diuretics. Initially, it begins with the spironolactone dose 100–200 mg once a day. The diuretic response was monitored

with 0.5 kg/day weight loss, without foot, or 1 kg/day edema with edema of the foot. Or inadequate spironolactone administration can be combined with furosemide at a dose of 20-40 mg/day. Administration of furosemide dosage may be increased if there is no response; maximum dose of 160 mg/day [7].

METHODS

Research design

This study was conducted with a prospective cross-sectional study design on spironolactone and its combination with furosemide at RSUP H. Adam Malik Medan, using urine Na/K examination and 24-h urine sodium. The study was analyzed statistically using Mann-Whitney U-test, SPSS Statistic program version 22.

Data source

The research sources were medical records of liver cirrhosis patients with accompanying ascites receiving SIRS (hospital information system) records of nurses in inpatient rooms, patient interview records, and clinical pathology laboratory examinations.

Time of study

The study was conducted in the hospitalization of Rindu A, Rindu B, and RIC in RSUP H. Adam Malik Medan.

Population and sample

Population

The population in this study was all patients with liver cirrhosis accompanied by ascites in the hospitalization of Rindu A, Rindu B, and RIC in RSUP H. Adam Malik Medan.

Sample

The samples in this study were populations that met the inclusion criteria and did not meet the exclusion criteria.

The inclusion criteria are*Inclusion criteria*

- Patients with cirrhosis of the liver accompanied by ascites who are hospitalized internal wards integrated diagnostic installation diagnosed by anamnesis, physical examination and laboratory, and diuretic therapy received at least 1 day
- Willing to be the object of research by signing informed consent
- The type of diuretic used in the treatment of spironolactone and its combination with furosemide.

Exclusion criteria

Patients who are not allowed to participate in this study, if they have:

- Kidney abnormalities, as evidenced by serum creatinine <1.5 mg/dL
- Refused to participate
- Not using spironolactone
- Does not use the combination with furosemide.

Number of samples

The sample size was the number of liver cirrhosis patients with inpatient ascites receiving spironolactone therapy and its combination with furosemide, calculated according to the Raosoft program [8] with the following values:

- The margin of error = 10%
- Confidence level = 90%
- Total population (population size) = 41
- (SIRS installation data 2016 RSUP H. Adam Malik Medan)
- Response distribution (response distribution) = 50%

- Then obtained a large sample of at least: 26 people.

Tools and materials*Tools used*

- 9180 electrolyte analyzer
- Cup sample
- Scientific term
- Bottle
- Pispot.

Materials used

- Sodium urine 24 h
- Na/K urine at the time
- Toluene
- Urine diluent.

Research steps

The steps of this research are carried out as follows:

- The research was conducted after obtaining informed consent, approved by Ethical Research Commission of health field of Faculty of Medicine, University of Sumatera Utara, and got approval from the director of RSUP H. Adam Malik Medan.
- Data collection of all spironolactone therapy and its combination with furosemide given in liver cirrhosis patients with ascites of inpatient based on Formulary of RSUP H. Adam Malik Medan, list of Jamkesmas diuretic drugs.
- Choose patients who meet inclusion criteria.
- Data retrieval.s

Research procedures

The materials examined were 24-h urine sodium and Na/K as collected in Gergen (24-h urine sodium) and in the bottle (Na/K urine at a time), which were examined by an electrolyte analyzer using the ion selective electrode (ISE) method. Measurement of this tool is using ISE or ISE. Where in this tool, there are four pieces of electrode that is Na electrode, K electrode, Cl electrode, and reference electrode. Electrolyte analyzer can detect inorganic salt ions, small calcium ion material

samples. The electrolyte working system is when electrolyte ions enter the electrode arising electrical potentials proportional to the electrolyte ion concentration. Then, the electric potential is corroborated and converted through the processor to the value of electrolyte concentration. The working principle of this tool that the sample will be drawn by electrodes that are sensitive to these ions. Then, a reference electrode is used to compare potential ups and downs [9].

The data collected in this research are

- Records of medical record data at inpatient Rindu A, Rindu B, and RIC at RSUP H. Adam Malik Medan include data of demographic characteristics of patients (name, gender, age, and ethnicity).
- Patient data related to each criterion of liver cirrhosis accompanied by ascites, drug selection.
- Patient laboratory data, recorded after diuretic administration. Assessment/measurement of urine sodium 24 h.
- Patient laboratory data, recorded after diuretic administration. Assessment/Measurement of urine sodium 24 hours and Na/K urine at a time, was done by compared 24-hour urine sodium using spironolactone and its combination with furosemide and compared with Na/K urine when using spironolactone and its combination with furosemide.
- The captured data were moved to the data collection sheets. Lack of medical record data was supplemented by looking at nurse records, SIRS data (Hospital Information System), and looking at the patient's condition.

Data analysis

The data obtained are presented in table form, then analyzed statistically using Mann-Whitney U-test, SPSS Statistic program version 22.

RESULT AND DISCUSSION**RESULTS**

A prospective cross-sectional study was conducted on liver cirrhosis patients with ascites using spironolactone and its combination with furosemide in the RSUP H. Adam Malik Hospital Medan from June 2017 to September 2017 with 24-h urine sodium and urine Na/K.

Demographic characteristics of research subjects

Based on the number of samples, there are as many as 26 patients with liver cirrhosis accompanied ascites that have met the inclusion; as many as 17 patients (65.38%), men aged 20–81 years, while women as many as 9 patients (34.61%), with age 30–67 years; mostly from tribe of Batak 13 people (50%), Javanese 10 patients (38.46%), and Malay 3 patients (11.53%). The study was divided into two groups of patients, Group I using a single drug (spironolactone) of 9 patients; men 5 people (55.55%), while women 4 patients (44.44%); with age 20–81 years, Batak 2 (22.22%), Javanese 6 (66.66%), and Malay 1 (11.11%). Group II used its combination with furosemide of 17 patients, 12 patients (70.58%), 5 (29.41%), age 39–65; Batak tribe 11 (64.70%), Java 4 (23.52%), and Malay 2 (11.76%).

To determine what statistical tests were used for the spironolactone group and its combination with furosemide, the normality test was first performed. The test data of normality of Na/K urine can be seen in Table 1, Sodium Urine Value Result When Using Mann-Whitney Test seen in Table 2, 24-hour urine sodium normality test data can be seen in Table 3, and 24-hour Sodium Urine Value Using the Mann-Whitney Test seen in Table 4.

DISCUSSION

The population of this study was 26 patients, most of the patients in RSUP H. Adam Malik Medan were male patients, amounted to 17 (65.38%) patients, while women were 9 (34.61%) patients. In this study, the patients used spironolactone and its combination with furosemide, which used spironolactone as many as 9 patients, from 9 patients were men, 5 patients, women 4 patients aged patients ranged

from 39-65 year. While using combination with furosemide as many as 17 male patients amounted to 12 patients, women 5 patients with age ranged from 20 to 81 years. Overall, there were more male patients than women. Liver cirrhosis is a major risk factor for liver cancer in the world and underlies more than 80% of cases of liver cancer. Every year 3-5% of patients with liver cirrhosis will have liver cancer. Moreover, liver cancer is one of the causes of death in cirrhosis of the liver; the time it takes cirrhosis of the liver to develop into liver cancer is about 3 years. Alcohol consumption is a risk factor for cirrhosis of the liver. Alcohol-heavy drinkers (more than 50-70 g/day and prolonged) are at risk for liver cancer through alcoholic liver cirrhosis, the mechanism of liver disease due to alcohol consumption is uncertain, liver cells undergo prolonged fibrosis and protein destruction due to alcohol metabolism that results in acetaldehyde. Fibrosis that occurs stimulates the formation collagen. Regeneration of cells still occurs but cannot compensate for cell damage. The accumulation of collagen continues, the size of the liver narrows, lumps, and hardened resulting in cirrhosis of the liver [10].

In liver cirrhosis with ascites, spironolactone response to liver cirrhosis patients accompanied ascites, with urine Na/K examination with normal values >1 mEq result of good response laboratory value, while 24 hours urine suture test 3 patients less responsive to the value <78 mEq. Spironolactone is widely used for the treatment of liver cirrhosis ascites complications [11]. While the combined response with furosemide with urine Na/K examination when the response is good to the value >1 mEq. A 24-h urine sodium examination had two patients <78 mEq. Based on the results, it was concluded that the combination with furosemide was better than spironolactone. Its combination with furosemide is widely used for the treatment of liver cirrhosis to enlarge diuresis.

After test with Mann-Whitney U statistic test and compared urine Na/K examination during spironolactone and Na/K urine during combination with furosemide, it was obtained that Asymp. significance (2-tailed) 0.435 value was statistically no significant difference. Moreover, 24 h of urinary sodium test against spironolactone compared with its combination with furosemide. Asymp. significance (2-tailed) 0.628 value shows no significant difference between spironolactone and its combination with furosemide based on the significance (2-tailed) value obtained >0.05, i.e. 0.435 for Na/K urine and 0.628 for 24-h urine sodium.

According to [12], the principle of treating liver cirrhosis ascites complications is to make the balance of abnormal sodium, one of them with the use of diuretics; the use of diuretics in the treatment of therapy is done immediately by considering the low efficacy of sodium diet restriction. The purpose of diuretic use was to evaluate the effectiveness of diuretics on the development of liver cirrhosis response to ascitic complications. Previous studies have compared spironolactone and its combination with furosemide, which used spironolactone 8 patients and used a combination of spironolactone with furosemide 27 patients. Administration of diuretics effectively decreases ascites in cirrhosis of the liver seen from the circumference of the stomach and the patient's weight. Based on the results statistics

no significant difference between spironolactone and combination of spironolactone with furosemide.

Cirrhosis is a complication of liver disease characterized by the disappearance of liver cells and the formation of connective tissue in the liver that is irreversible. Alcohol and viral hepatitis B and C are the leading cause of liver cirrhosis, although there are many other causes. Cirrhosis can cause weakness, loss of appetite, itching, and fatigue. Suspected cirrhosis on the basis of anamnesis, physical examination, and blood tests, cirrhosis is confirmed by liver biopsy. Complications of cirrhosis include edema, ascites, and liver cancer. Treatment of liver cirrhosis aims to prevent further liver damage, treat complications, and prevent liver cancer. Moreover, liver transplantation is now one of the important options for the treatment of advanced liver cirrhosis patients.

CONCLUSION

Based on observations during the study and discussion, it can be concluded: The combination of spironolactone with furosemide was better than spironolactone although statistically there was no significant difference, better laboratory result of spironolactone combination with furosemide was seen from the comparison of 24-h urine sodium value with normal value of 78 mEq.

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