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Furosemide Use in Chronic Kidney Disease Patients

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Abstract.
Chronic kidney disease is defined as kidney disease occurring for more than three months and is characterized by a decreasing glomerular filtration rate, reaching below 60 mL/min/1.73 m^2. Decreased kidney function can reduce the kidney's capacity to excrete sodium. Excess extracellular fluid will cause hypertension, and lower and upper extremity edema. Loop diuretics, such as furosemide, are known to increase sodium excretion by 20%, thereby reducing the amount of extracellular fluid. This study aimed to determine the patterns of furosemide use in chronic kidney disease patients at University of Muhammadiyah Malang General Hospital. Observational, descriptive, and retrospective data collection methods were used. The use of a single furosemide pattern was given to 25 patients (40%); a two-combination to 12 patients (20%); a three-combination to 9 patients (15%); a four-combination to 12 patients (20%); and a five-combination to 4 patients (5%). The most commonly used single furosemide was furosemide (3 x 40 mg, intravenous [iv]), which was administered to 16 patients (73%); the most common two-combination was furosemide (3 x 40 mg, iv) + amlodipine (1 x 10 mg, oral), which was given to 2 patients (20%); the most common three-combination was furosemide (3 x 40 mg, iv) + candesartan (1 x 16 mg, oral) + amlodipine (1 x 5 mg) and furosemide (3 x 40 mg, iv) + candesartan (1 x 16 mg, oral) + amlodipine (1 x 10 mg, oral), which was given to 2 patients (23%); the most common four-combination was furosemide (3 x 40 mg, iv) + nifedipine (3 x 10 mg, oral) + clonidine (3 x 0.15 mg, oral) + captopril (2 x 25 mg, oral), which was given to 3 patients (28%); and the most common five-combination was given to 1 patient (25%) with 4 patterns. In short, there were 22 patterns of furosemide switch therapy.

Keywords: furosemide, edema, chronic kidney disease

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1. Introduction

Chronic Kidney Disease (CKD) is defined as an abnormality or disorder of the kidneys, both the structure and function, for more than three months. Abnormalities in CKD patients are characterized by albuminuria, hematuria, electrolytes, histology, renal structure, or a history of kidney transplantation. The classification of Chronic Kidney

Disease (CKD) is also based on the cause of the disease, the category of glomerular filtration rate (GFR), and the level of albuminuria [1].

In 1990, CKD was ranked 27^{th} as the leading global cause of death, but in 2010 CKD climbed up to the 18^{th} [2]. According to the National Institute of Diabetes and Digestive and Kidney Disease (NIDDKD), the prevalence of CKD among the age group of 20-64 years is 0.5%, while the incidence rate at the age older than 65 years reaches 4.3% [3]. Based on data reported by the United States Renal Data System (USRDS) (2015) in 2013, among the United States population, there were 117,162 cases of CKD. Meanwhile, in 2013, the prevalence of CKD in Indonesia also increased to 499,800. Moreover, Basic Health Research data recorded at the Ministry of Health shows the prevalence of CKD in men is higher than women, which were 0.3% and 0.2%, respectively [4].

CKD patients may increase the progression of COVID-19 to become more severe. Patients with CKD are also known to have a higher mortality rate when compared to non-CKD patients. CKD causes changes in the immune system, such as persistent systemic inflammation and acquired immunosuppression. Characterized by dysfunction of cell phagocytosis and increased concentrations of pro-inflammatory cytokines and inflammatory monocytes. The presence of persistent inflammation is a risk factor for the development of CKD and cardiovascular disease. In addition, CKD patients who have comorbidities such as diabetes mellitus and hypertension can also aggravate the severity of COVID-19 [5]. According to research by Huang et al, the most common comorbidities found in COVID-19 patients were diabetes (20%), hypertension (15%), and cardiovascular disease (15%). Due to the high percentage of comorbid hypertension, many experts have begun to argue about the use of hypertension drugs that block the renin-angiotensin-aldosterone system (RAAS). Two factors that influence this debate. First, the results of observations show that hypertensive patients with severe cases of COVID 19 who are undergoing treatment at the hospital have a risk of dying. Second, one study stated that the etiology of COVID 19 is SARS-CoV-2 which has a specific site for angiotensin-converting enzyme 2 (ACE2) which is abundant in the heart and lungs [6].

Clinical manifestations often experienced by CKD patients are hypertension, hyponatremia, hyperkalemia, hyperphosphatemia, metabolic acidosis, edema, and anemia [7]. In general, CKD patients will also experience uremia, symptoms such as nausea, vomiting, body weakness, shortness of breath, edema, and fatigue. Therapy in CKD aims to prevent and inhibit the occurrence of severe complications and slow the worsening kidney damage [1].

A progressive decline in kidney function can decrease the kidneys' capacity to excrete Na. Excess extracellular fluid will cause lower extremity edema and hypertension. Therefore, the therapy widely used in the hypertension management of CKD patients is the administration of the diuretic drug. Loop diuretics such as furosemide increase Na excretion by 20%, thus reducing the amount of extracellular fluid [8]. Other loop diuretic drugs are furosemide, bumetanide, pyrethanide, ethacrynic acid, and ethozoline. However, in CKD patients, furosemide is the most widely prescribed loop diuretic drug [9]. Management of CKD is not only aimed at treating the main causes of kidney disorders but also to minimize concomitant conditions or complications and slowing the decline in kidney function [10].

2. Research Methods

This study applied an observational descriptive research design on the use of furosemide in chronic kidney disease (CKD) patients. Data collection was carried out retrospectively by processing Health Medical Record data of CKD patients at University of Muhammadiyah Malang General Hospital from January 1 to December 31, 2020.

3. Results And Discussion

Based on research conducted on CKD patients at University of Muhammadiyah Malang Hospital using Health Medical Record data from January 1 to December 31, 2020, of the 80 populations, a total of 39 samples that received furosemide therapy in CKD patients and met the inclusion criteria were obtained.

3.1. Patient Demographic Data

Based on **Table 1**, the highest incidence of CKD is at the age group of 55-64 years (33%). Along with the increasing age, kidney function will decrease, starting from the kidneys' anatomy, physiology, and cytology. The kidneys of a person older than 30 years old will undergo atrophy, and the thickness of the renal cortex will decrease by up to 20% every 10 years [11].

Based on **Table 2**, most CKD patients were male, as many as 23 patients (53%). An epidemiological study conducted by Weinstein and Anderson (2010) showed that decreased kidney function in men could be caused by an unhealthy lifestyle and smoking (Weinstein and Anderson, 2010 in Arianti, Rachmawati, & Marfianti, 2020).

Table 1: Patients with CKD by Age Group.

Range	Total	Percentage (%)
15-24 years	2	5
25-34 years	1	3
35-44 years	3	7
45-54 years	10	26
years	13	33
≥ 65 years	10	26
Total	**39**	**100**

Source: Basic Health Research 2018

Table 2: CKD Patients based on Gender.

Gender	Total	Percentage (%)
Male	23	53
Female	16	47
Total	**39**	**100**

In addition, the other factor is the reproductive hormones differences owned between men and women. The estrogen hormone in women can induce endothelial cells that are important for the kidneys to avoid reduced microvascular endothelium and hypoxia, or the estrogen hormone also functions as a nephroprotector [13].

Table 3: CKD Patients Mapping based on Insurance Status.

Insurance Status	Total	Percentage (%)
General Patient	1	3
BPJS	38	97
Total	**39**	**100**

Table 3 shows that CKD patients undergoing hospitalization are dominated by patients covered by BPJS (Social Security Administrator for Health), as many as 38 patients (97%). According to BPJS Health data in 2020, which includes the costs of catastrophic diseases borne by BPJS in 2019, kidney failure is the 4th leading disease with 1.8 million cases in a year [14].

3.2. Medical History

Table 4 shows that the prevalence of medical history of CKD patients were mostly Hypertension (50%) and Diabetes Mellitus (28%). Hypertension that happens for a long time and is not controlled will result in changes in the arterioles structure throughout the

Table 4: Medical History of CKD Patients.

Medical History	*	(%)
Hypertension	29	50
Diabetes Mellitus	16	28
Stroke	2	3
Heart disease	8	13
Uric Acid	1	2
Cholesterol	1	2
Lupus	1	2
Total	**58**	**100**

*A patient can have more than one disease

body. It will be characterized by fibrosis and hyalinization of blood vessel walls. When this happens, the organs that become the main targets are the heart, brain, kidneys and eyes. The conditions of the kidneys in patients with prolonged hypertension generally have atherosclerosis, which in the long term will cause nephrosclerosis (Masi & Kundre, 2018). It is known that the kidneys have many small blood vessels; thus, uncontrolled diabetes can damage the vessels and affect the kidneys' ability to filter the blood. This condition will cause albuminuria (Clovy, 2010, in Masi & Kundre, 2018).

3.3. Furosemide Usage Pattern

Table 5: The use of single furosemide therapy in patients with CKD.

Dosage Regimen	*	(%)
Furosemide (1 x 40 mg) IV	6	24
Furosemide (2 x 40 mg) IV	1	1
Furosemide (3 x 20 mg) IV	1	1
Furosemide (3 x 40 mg) IV	16	73
Furosemide (5 mg/Jam) IV Drip	1	1
Total	**25**	**100**

*One patient can have more than one therapeutic use

Based on **Table 5** the most widely used therapeutic use pattern is single furosemide (3 x 40 mg) iv. The administration of this therapeutic pattern depends on the patient's condition. In this study, patients who received single therapy in the hospital admission generally complained about shortness of breath, edema in either the feet or hands or even both, and slightly high blood pressure. Furosemide is the first-line drug that can be given to patients with edema that may occur due to increased RAAS activity. Diuretics can specifically reduce the reabsorption of sodium (Na^+) in the renal tubules so that

they can increase the excretion of sodium and water in the urine. In CKD patients, fluid accumulation or severe edema can occur due to decreased kidney function [16].

In JNC 8 Guidelines for the Management of Hypertension in CKD patients with or without diabetes mellitus, the blood pressure targets are <140 mmHg (systolic) and <90 mmHg (diastolic). The antihypertensive treatments are first-line (ACEI/ARB, which can be given alone or combined with other hypertension groups), second-line (ACEI/ARB, CCB, thiazide diuretics), and third-line (β-blockers, aldosterone antagonists, etc).

Management of hypertension is generally given ACEI or ARB. This raises many questions for experts considering that in COVID-19 patients infected with SARS-CoV-2, ACE2 will bind to the lungs and heart. The use of ACEIs and ARBs is thought to increase ACE2 in patients, thereby increasing the possibility of being infected with COVID 19 which can progress to become more severe. However, in a study conducted by Linelajan (2021), based on the results of a literature review, it was stated that ACEI and ARB antihypertensive therapy did not affect the outcome, mortality, and disease progression. However, it should be noted that the use of this therapy can provide benefits in reducing the mortality rate and outcomes of COVID-19 patients who have comorbid hypertension [6].

Table 6: Pattern of Two-Combination of Furosemide Therapy in CKD Patients.

Group	**Dosage Regimen**	□	**(%)**
Diuretic + CCB	Furosemide premed (1 x 40 mg) iv + Amlodipine (1 x 10 mg) po	1	10
	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po	1	10
	Furosemide (3 x 40 mg) iv + Amlodipine (1 x 10 mg) po	2	20
	Furosemide (3 x 40 mg) iv + Nicardipine (2.5 -7.5 mg/hour) iv	1	10
	Furosemide (3 x 40 mg) iv + Nicardipine (2.5 mg/hour) iv	1	10
Diuretic + β-Blocker	Furosemide (3 x 40 mg) iv + Bisoprolol (1 x 2.5 mg) po	1	10
Diuretic + ACEI	Furosemide premed (1 x 40 mg) iv + Ramipril (1 x 10 mg) po	1	10
	Furosemide (3 x 40 mg) iv + Ramipril (1 x 2.5 mg) po	1	10
Diuretic + ARB	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po	1	10
	Total	**10**	**100**

In **Table 6**, the pattern of furosemide therapy is mostly combined with CCB antihypertensive drugs. CCB will inhibit the process of moving calcium to cardiac muscle cells

and smooth muscle in blood vessel walls. It will also relax blood vessel muscles and reduce peripheral resistance, thus decreasing the blood pressure**.**

Table 7: Pattern of Three-Combination of Furosemide Therapy in CKD Patients.

Group	Dosage Regimen		(%)
Diuretic + ARB + CCB	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 5 mg) po	2	23
	Furosemide premed (1 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po	1	11
	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po	2	23
Diuretic + ACEI + β-Blocker	Furosemide premed (1 x 40 mg) iv + Ramipril (1 x 10 mg) po + Bisoprolol (1 x 2,5 mg) po	1	11
Diuretic + ACEI + CCB	Furosemide (2 x 40 mg) iv + Captopril (3 x 25 mg) po + Nifedipine (3 x 10 mg) po	1	11
Diuretic + Diuretic + ARB	Furosemide (3 x 40 mg) iv + Furosemide premed (1 x 40 mg) iv + Candesartan (1 x 16 mg) po	1	11
Diuretic + ARB + ACEI	Furosemide (2 x 40 mg) iv + Candesartan (1 x 8 mg) po + Amlodipine (1 x 10 mg) po	1	11
	Total	**9**	**100**

In **Table 7**, the most common pattern of three-combination of furosemide therapy is diuretic + ARB + CCB. ARBs have an action mechanism, namely occupying AT I receptors in blood vessels so that they can reduce the physiological effects of angiotensin. The choice of ARB in elderly patients is recommended because this class of drugs does not cause coughing as in the ACEI group.

Table 8 shows the pattern of four-combination of furosemide usage. In this combination, there is the addition of β-blocker antihypertensive drugs (Bisoprolol) and α-2 agonists (Clonidine). Administration of β-blocker is recommended as an antihypertensive drug in patients who have a history of heart disease. Then, the administration of α-2 agonist, such as clonidine, is the management for patients who have hypertensive emergencies. A hypertensive emergency is if the patient's blood pressure is above 180/120 mmHg [17].

In **Table 9**, some patients were given Furosemide Premedication therapy. Furosemide premedication will be given if the patient is receiving blood transfusion therapy or administered with PRC. In CKD cases, it is often known as Transfusion Associated Circulatory Overload (TACO). TACO occurs when the transfused volume results in

Table 8: Pattern of Four-Combination of Furosemide Therapy in CKD Patients.

Group	Dosage Regimen		(%)
Diuretic + CCB + α-Blocker + ACEI	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po	3	28
	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 5 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po	1	8
Diuretic + ARB + CCB + α-Blocker	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Clonidine (3 x 0,15 mg) po	1	8
	Furosemide premed (1 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Clonidine (3 x 0,15 mg) po	1	8
	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 5 mg) po + Clonidine (3 x 0,15 mg) po	1	8
Diuretic + ARB + CCB + β-Blocker	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Bisoprolol (1 x 5 mg) po	1	8
	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Bisoprolol (1 x 2,5 mg) po	1	8
Diuretic + CCB + ARB + ACEI	Furosemide (2 x 40 mg) po + Nifedipine (3 x 10 mg) po + Candesartan (1 x 16 mg) po + Captopril (3 x 25 mg) po	1	8
Diuretic + CCB + β-Blocker + ACEI	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Bisoprolol (1 x 5 mg) po + Captopril (2 x 25 mg) po	1	8
Diuretic + CCB + ACEI + CCB	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Captopril (2 x 25 mg) po + Amlodipine (3 x 10 mg) po	1	8
	Total	**12**	**100**

pulmonary edema, where the patients with pulmonary edema are more likely to experience respiratory distress, hypoxaemia, and increased venous pressure. Furosemide administration aims to reduce the risk of extremity edema and pulmonary edema [18].

Based on the study results in **Table 10** that shows the switching pattern of Furosemide usage, there is a switch in the therapy pattern based on the patient's clinical condition. The switching therapy also needs to pay attention to the drug combination, whether it has side effects and interactions between drugs. From this study, 22 patterns of switch therapy were obtained.

3.4. Duration of Furosemide Usage

Table 9: Pattern of Five-Combination of Furosemide Therapy in CKD Patients.

Group	Dosage Regimen	□	(%)
Diuretic + Diuretic + CCB + α-Blocker + ACEI	Furosemide (3 x 40 mg) iv + Furosemide premed (1 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po	1	25
Diuretic + α-Blocker + ACEI + β-Blocker + CCB	Furosemide (3 x 20 mg) iv + Clonidine (3 x 0,15 mg) po + Captopril (3 x 25 mg) po + Bisoprolol (1 x 5 mg) po + Diltiazem (3 x 30 mg) po	1	25
	Furosemide (2 x 40 mg) po + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (3 x 25 mg) po + Bisoprolol (1 x 5 mg) po	1	25
Diuretic + CCB + ACEI + CCB + β-Blocker	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Captopril (2 x 25 mg) po + Amlodipine (3 x 10 mg) po + Bisoprolol (1 x 2,5 mg) po	1	25
	Total	**4**	**100**

Table 10: Furosemide Switching Pattern.

No. Sample	Pattern 1		Pattern 2	Pattern 3	Pattern 4	∑	%
	Single		**Four-combination**				
3	Candesartan (1 x 16 mg) iv	→	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Clonidine (3 x 0,15 mg) po			1	4
	Two-combination		**Four-combination**				
4	Amlodipine (1 x 10 mg) po + Candesartan (1 x 16 mg) po	→	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Bisoprolol (1 x 5 mg) po			1	4
	Single		**Three-combination**				
10	Furosemide premed (1 x 40 mg) iv	→	Amlodipine (1 x 10 mg) po + Candesartan (1 x 16 mg) po + Bisoprolol (1 x 5 mg) po			1	4
	Single		**Four-combination**				
14	Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 5 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po			1	4
	Single		**Single**				
16	Furosemide premed (1 x 40 mg) iv + Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv			1	4
	Single		**Two-combination**				
17	Bisoprolol (1 x 2,5 mg) po	→	Furosemide (3 x 40 mg) iv + Bisoprolol (1 x 2,5 mg) po			1	4
	Single		**Four-combination**				
21	Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po			1	4
	Single		**Three-combination**				
25, 36	Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po			2	16
	Two-combination		**Four-combination**				
28	Furosemide (3 x 40 mg) iv + Nicardipine (2,5 -7,5 mg/jam) iv	→	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Bisoprolol (1 x 5 mg) po + Captopril (2 x 25 mg) po			1	4
	Single		**Two-combination**				
29	Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv + Amlodipine (1 x 10 mg) po			1	4
	Single		**Single**				
31	Furosemide (3 x 40 mg) iv	→	Furosemide premed (1 x 40 mg) iv + Furosemide (3 x 20 mg) iv			1	4

Table 10: (Continued).

No. Sample	Pattern 1		Pattern 2	Pattern 3	Pattern 4	∑	%
	Two-combination		**Three-combination**				
32	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po	→	Furosemide (3 x 40 mg) iv + Furosemide premed (1 x 40 mg) iv + Candesartan (1 x 16 mg) po			1	4
	Single		**Three-combination**				
39	Furosemide (2 x 40 mg) iv	→	Furosemide (2 x 40 mg) iv + Candesartan (1 x 8 mg) po + Amlodipine (1 x 10 mg) po			1	4
	Two-combination		**Five-combination**	**Four-combination**			
2	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po	→	Furosemide (3 x 40 mg) iv + Furosemide premed (1 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po	–Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (2 x 25 mg) po		1	4
	Two-combination		**Four-combination**	**Two-combination**			
13	Candesartan (1 x 16 mg) po + Clonidine (3 x 0,15 mg) po	→	Furosemide premed (1 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Clonidine (3 x 0,15 mg) po	–Candesartan (1 x 16 mg) po + Clonidine (3 x 0,15 mg) po + Amlodipine (1 x 10 mg) po		1	4
	Two-combination		**Single**	**Single**			
15	Nifedipine (3 x 5 mg) po + Captopril (2 x 25 mg) po	→	Furosemide (5 mg/jam) iv drip	–Furosemide (3 x 20 mg) iv		1	4
	Single		**Two-combination**	**Three-combination**			
20	Furosemide premed (1 x 40 mg) iv	→	Furosemide premed (1 x 40 mg) iv + Ramipril (1 x 10 mg) po	–Furosemide premed (1 x 40 mg) iv + Ramipril (1 x 10 mg) po + Bisoprolol (1 x 2,5 mg) po		1	4
	Four-combination		**Three-combination**	**Five-combination**			
26	Furosemide (2 x 40 mg) po + Nifedipine (3 x 10 mg) po + Candesartan (1 x 16 mg) po + Captopril (3 x 25 mg) po	→	Furosemide (2 x 40 mg) iv + Captopril (3 x 25 mg) po + Nifedipine (3 x 10 mg) po	–Furosemide (2 x 40 mg) po + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0,15 mg) po + Captopril (3 x 25 mg) po + Bisoprolol (1 x 5 mg) po		1	4

Table 10: (Continued).

No. Sample	Pattern 1		Pattern 2	Pattern 3	Pattern 4	∑	%
	Single		**Three-combination**	**Four-combination**			
30	Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 5 mg) po	– Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 5 mg) po + Clonidine (3 x 0,15 mg) po		1	4
	Single		**Four-combination**	**Two-combination**			
34	Furosemide (3 x 40 mg) iv	→	Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po + Bisoprolol (1 x 2,5 mg) po	– Furosemide (3 x 40 mg) iv + Ramipril (1 x 2,5 mg) po		1	4
	Two-combination		**Four-combination**	**Five-combination**			
37	Furosemide (3 x 40 mg) iv + Nicardipine (2,5 mg/jam) iv	→	Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Captopril (2 x 25 mg) po + Amlodipine (3 x 10 mg) po	– Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Captopril (2 x 25 mg) po + Amlodipine (3 x 10 mg) po + Bisoprolol (1 x 2,5 mg) po		1	4
	Single		**Two-combination**	**Four-combination**	**Five-combination**		
11	Nicardipine (2,5 mg/jam) iv drip	→	Captopril (3 x 25 mg) po + Diltiazem (3 x 30 mg) po	– Captopril (3 x 25 mg) po + Diltiazem (3 x 30 mg) po + Clonidine (3 x 0,15 mg) po + Bisoprolol (1 x 5 mg) po	– Furosemide (3 x 20 mg) iv + Clonidine (3 x 0,15 mg) po + Captopril (3 x 25 mg) po + Bisoprolol (1 x 5 mg) po + Diltiazem (3 x 30 mg) po	1	4
Total						**23**	**100**

Table 11: Duration of Furosemide Usage.

Duration of Therapy	Result	
	Total	**Percentage (%)**
1 – 5 days	32	82
6 – 10 days	7	18
Total	**39**	**100**

Based on the results in **Table 11**, the most common duration of furosemide therapy given to CKD patients at the Muhammadiyah University Hospital Malang is 1-5 days, given to as many as 32 patients (82%).

3.5. Length of Inpatient Care

TABLE 12: Length of Inpatient Care.

Length of Care	Result	
	Total	Percentage (%)
1 – 5 days	28	72
6 – 10 days	11	28
Total	**39**	**100**

In **Table 12** the study results found that the most common duration of treatment for CKD patients at University of Muhammadiyah Malang Hospital was 1-5 days, with a total of 28 patients (72%).

3.6. Conditions at Hospital Discharge

TABLE 13: Patient's Condition at Hospital Discharge.

Conditions at Hospital Discharge	Result	
	Total	Percentage (%)
Improved	37	95
Died	2	5
Total	**39**	**100**

Table 13 shows that 37 patients were in improved condition at hospital discharge, and 2 other patients passed away.

4. Conclusion

1. The use of a single furosemide pattern was given to 25 patients (40%), a two-combination to 12 patients (20%), a three-combination to 9 patients (15%), a four-combination to 12 patients (20%), and a five-combination to 4 patients (5%).

2. The mostly used single Furosemide was the Furosemide (3 x 40 mg) iv as many as 16 patients (73%), the two-combination was Furosemide (3 x 40 mg) iv + Amlodipine (1 x 10 mg) po as many as 2 patients (20%), the three-combination was Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 5 mg) and Furosemide (3 x 40 mg) iv + Candesartan (1 x 16 mg) po + Amlodipine (1 x 10 mg) po as many as 2 patients each (23%), the four-combination was Furosemide (3 x 40 mg) iv + Nifedipine (3 x 10 mg) po + Clonidine (3 x 0.15 mg) po + Captopril (2 x 25 mg) po as many as 3 patients (28%), and the five-combination was 1 patient (25%) with 4 patterns.
3. There are 22 patterns of Furosemide switch therapy.

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