UNDERGRADUATE THESIS

EVALUATION OF ANTIHYPERTENSIVE DRUG USAGE IN CKD OUTPATIENTS WITH HEMODIALYSIS AT RSUP DR. SOERADJI TIRTONEGORO KLATEN 2017

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STATEMENT OF ELIGIBILITY
FOR UNDERGRADUATE THESIS EXAMINATION

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EVALUATION OF ANTIVIRUS RESISTIVE DRUG USE IN CD4
OUTPATIENTS WITH HEPTOSIS AT ISUU DR SERARI

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I hereby that this thesis originally belongs to my own work and does not belong to another researcher of a different degree. Furthermore, this thesis is never published before, except some parts of their original references.

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بسم الله الرحمن الرحيم

السلام عليكم ورحمة الله وبركاته

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والسلام عليكم ورحمة الله وبركاته

Ngawi, Sya‘ban 18th, 1439 H
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Fatihah Affiah
ABSTRACT

Hypertension is one of the major risk factors for chronic renal failure because it can cause damage to blood vessels in the kidney, thus reducing the ability of the kidneys to filter blood properly. Giving and analyzing antihypertensive drugs are very important in these circumstances, as it can accelerate the progression of the disease and increase the patient’s mortality rate. Rasulullah sallallaahu ‘alaihi wasallam, said: ‘There is a cure for every disease’. If the medicine is right for an illness, it will be healed with the permission of Allah ‘Azza wajalla “(H.R. Muslim). Therefore, the aspects of efficacy and safety of drug use in patients need to be evaluated. The purpose of this study was to determine patient accuracy, drug accuracy and dose accuracy evaluated based on reference books in the use of antihypertensive therapy in outpatients with chronic renal failure with hemodialysis. This research is a descriptive research conducted at RSUP dr. Soeradji Tirtonegoro Klaten. Data were retrospective from medical records, using non-experimental methods. The patient sample was taken according to the inclusion criteria of the research by purposive sampling method. The results of this study indicate that there were 55 patients evaluated consisted of 35 men (64%) and 20 women (36%). Based on the data obtained it can be concluded that the use of antihypertensive drugs in chronic renal failure outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017 shows right patient (100%), exact medicine (90,92%) and exact dose (98,19%).

Keywords: Antihypertensive, Outpatient, CKD, Hemodialysis
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-I</td>
<td>Angiotensin Converting Enzyme Inhibitor</td>
</tr>
<tr>
<td>AINS</td>
<td>Anti Inflamasi Non Steroid</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin Receptor Blocker</td>
</tr>
<tr>
<td>ARF</td>
<td>Acute Renal Failure</td>
</tr>
<tr>
<td>ASH</td>
<td>American Society of Hypertension</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BPH</td>
<td>Benign Prostatic Hyperpalsia</td>
</tr>
<tr>
<td>BPOM</td>
<td>Badan Penyelidik Obat dan Makanan</td>
</tr>
<tr>
<td>BUN</td>
<td>Blood Urea Nitrogen</td>
</tr>
<tr>
<td>CCB</td>
<td>Calcium Channel Blocker</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary Heart Disease</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic Kidney Disease</td>
</tr>
<tr>
<td>CRF</td>
<td>Chronic Renal Failure</td>
</tr>
<tr>
<td>DBP</td>
<td>Diastolic Blood Pressure</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>DNA</td>
<td>Asam Deoksiribonukleat</td>
</tr>
<tr>
<td>EDRF</td>
<td>Endothelium Derived Relaxing Factor</td>
</tr>
<tr>
<td>GFR</td>
<td>Gromerular Filtration Rate</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>HCT</td>
<td>Hidroklorotiazid</td>
</tr>
<tr>
<td>HDL</td>
<td>High Density Low</td>
</tr>
<tr>
<td>IRR</td>
<td>Indonesian Renal Registrasy</td>
</tr>
<tr>
<td>JNC</td>
<td>Joint National Committee</td>
</tr>
<tr>
<td>KDOQI</td>
<td>Kidney Disease Outcomes Quality Initiative</td>
</tr>
<tr>
<td>LDL</td>
<td>Low Density Lipoprotein</td>
</tr>
</tbody>
</table>
LVH  : Left Ventricular Hyperthropy
NSAIDs : Nonsteroidal Anti-Inflammatory Drugs
SBP  : Sistolic Blood Pleasure
SLE  : Systemic Lupus Erythematous
CHAPTER 1
INTRODUCTION

1.1. Background

Hypertension is a disease that is often found in the world of health. Hypertension is also a major risk factor for acute renal failure and chronic renal failure as it can lead to damage to blood vessels in the kidneys, thus reducing the ability of the kidneys to fine-tune blood (Guyton, 2006). The occurrence of kidney damage, heart to stroke is a cause of hypertension disease in the long term (Kementrian Kesehatan RI, 2014). Provision of antihypertensive drugs is very important in patients who have a hypertensive disease with renal failure undergoing hemodialysis. Hypertension can accelerate the progression of the disease and increase the mortality rate of patients with renal failure who undergo hemodialysis. Thus, it can be concluded how important the provision of antihypertensive drugs for patients with hemodialysis with these conditions (National Kidney Foundation, 2002).

The kidneys function by regulating the water balance, the concentration of salt in the blood and the removal of waste and excess salt. While kidney failure is an abnormality in the kidney, it is where the harmful substances begin to accumulate in the body, blood pressure becomes high, and the fluid becomes excessive (Irianto, 2012).

Indonesia is one of the countries that each year has increased patients suffering from chronic renal failure. Data recorded by ASKES, in 2010 there were 17,507 patients with chronic renal failure, the following year there were 23,261 patients and by 2013 there were 24,141 patients with chronic renal failure (Mailani, 2015). In 2013, 0.2% or 504,248 Indonesians suffer from chronic renal failure with a population of 252,124,458 people (Kementrian Kesehatan RI, 2013).
Chronic renal failure is a renal impairment in the form of structural or functional abnormalities with or without a decrease in GFR (Glomerular Filtration Rate) for more than 3 (three) months. Glomerular filtration rate is less than 60 ml/min 1.73 m$^2$ with or without damage on the kidneys for 3 (three) months. If there is kidney damage for more than three months and glomerular filtration rate is equal to or more than 60 ml/min 1.73 m$^2$, it does not include the criteria for chronic renal failure (Suwitra, 2007).

Jabir bin ‘Abdullah radhiyallahu ‘anhu, from Rasulullah Shallallahu ‘alaihi wasallam, that he said:

بِإِذْ اللهِ عَزَّ وَ جَلَّ صِيْبَ دَوَاءُ الدَّاءِ بَرَأَ دَاءٍ دَوَاءُ، فَإِذَا أُصِيبَ دَوَاءُ الدَّاءِ بَرَأَ يَاذَنِ اللهِ عَرَ وَ جَلَّ رواه  مسلم

Which means: “There is a cure every disease. If the medicine is right for an illness, it will be healed with the permission of Allah ‘Azza wajalla” (H.R. Muslim).

From the above hadith it can be concluded that in drinking or consuming a drug it should be precise, safe and rational. Because if the medicine is right for a disease it will heal with the permission of Allah. In the use of drugs, it is necessary to evaluate them to be safe, effective and rational. Management of therapy in patients with chronic renal failure who undergo hemodialysis requires special attention to the accuracy of the drug, patient accuracy and precision of dosage.

A study conducted by Supadmi (2011) on the evaluation of the use of antihypertensive drugs in chronic renal failure patients undergoing hemodialysis concluded that there was an inappropriateness in patients taking captopril in 9 of 34 patients (Supadmi, 2011). Evaluating drug use is a continuous proces with the aim of ensuring the right, safe and effective medication. Therefore, the use of antihypertensive drugs in patients with
chronic renal failure undergoing hemodialysis needs to be monitored and evaluated to ensure safe, appropriate and rational use of drugs. Evaluation of the use of antihypertensive drugs in this study included patient accuracy, drug accuracy, and accuracy of dosage.

No matter what any medicine or a specialist has done, but if Allah does not want to heal then it will not be healed. So it can be concluded that medicine and doctors are just a way of healing, while healing is only coming from Allah Subhanallah wata’ala because Allah has declared that “He created everything”.

1.2. Formulation of The Problem
Looking at the background of the problem, a problem can be formulated as follows:

1. How is patient accuracy in the use of antihypertensive drugs in CKD outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017?

2. How is the accuracy of drug in the use of antihypertensive drugs in CKD outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017?

3. How is the accuracy of dosage in the use of antihypertensive drugs in CKD outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017?

1.3. Objectives of Research
1. To know the accuracy of patients in the use of antihypertensive drugs in CKD outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten in 2017.

2. To know the accuracy of drugs in the use of antihypertensive drugs in CKD outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten in 2017.

3. To know the accuracy of dosage in the use of antihypertensive drugs in

1.4. Benefits of Research

1.4.1. Theoretical Significance
1. As a reference source for further investigators related to evaluating the use of antihypertensive drugs in chronic renal failure outpatients with hemodialysis.
2. Providing knowledge to the public about the appropriate use of antihypertensive drugs.

1.4.2. Practical Significance
1. As a source of information and knowledge for pharmacists and other health workers.
2. It can broaden the horizons for pharmacists and other health workers on the proper use of antihypertensive drugs.
CHAPTER 2
LITERATURE REVIEW

2.1. Previous Research

A similar study was conducted by Winalda (2016) on the evaluation of the accuracy of drug therapy in patients with renal failure at the “X” Hospital in 2014. It can be obtained that the exact patient is 98.05%, the exact drug is 78.25%, the exact dose is 52.32% and a moderate dose of 65.53% hemodialysis. The difference with previous research is that this study is more specific on the antihypertensive treatment of outpatients with chronic renal failure undergoing hemodialysis.

In a previous study conducted by Fakhrunnisa (2016) on the evaluation of the use of antihypertensive drugs in chronic renal failure patients with hemodialysis in 2015, it can be obtained that the exact dosage results when they are not in hemodialysis is 93.10%, in which the appropriate doses while doing hemodialysis is 58.62%. The difference with previous research is that this study is more specific in patients who undergo ambulatory and that is used patient samples in 2017.

Similar research has also been conducted by Hendarti (2016) with the title of Evaluation of Drug Accuracy and Dosage of Antihypertensive Drugs in outpatient Hypertensive Patients at Ciputat Puskesmas in January-March 2015. The difference with previous research is that in this research it is more specific in patients with chronic renal failure with hemodialysis and samples taken in 2017 at RSUP dr. Soeradji Tirtonegoro Klaten.

Supporting the above three studies, it is necessary to analyze the accuracy of patients, medications, and doses of antihypertensive drugs in chronic renal failure patients with hemodialysis because the analysis is necessary to prevent the occurrence of cardiovascular complications which is the highest cause of death in hemodialysis patients. There needs to do
more specific research on the evaluation of antihypertensive drug use in chronic renal failure outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017.

2.2. Theoretical Basis
2.2.1. Kidney

The kidneys have a shape like bean organs located on both sides of the vertebral column. The right kidney is slightly lower than the left kidney as it is pressed downward by the liver (Price and Wilson, 2005). The kidneys in the body function in maintaining the water balance in the body, the osmolarity of the body fluids especially the water balance, regulating the amount and concentration of CES ions including sodium, chloride, potassium, calcium, hydrogen ions, bicarbonate, phosphate, sulfate and magnesium; maintaining plasma volume, maintaining acid-base balance in the body, excreting the rest of the body’s metabolism, producing erythropoietin, producing renin, and converting vitamin D into its active form (Sherwood, 2014).

![Figure 2.1 Nephrons and their components](Source: Sherwood, 2014)
Each kidney consists of 1 million microscopic functional units commonly called nephrons which are joined together by connective tissue. Nephrons are the smallest unit present in an organ capable of forming urine. The arrangement of the nephrons in the kidney produces two distinct regions, the outer region is called the renal cortex and the inner region is called the renal medulla. Each nephron consists of a vascular component and a tubular component, both of which are closely related structurally and functionally. The vascular component consists of afferent arterioles, glomerular, efferent arterioles, and peritubular capillaries. Afferent arterioles serve to carry blood to the glomerular while the efferent arterioles serve to carry blood from the glomerular. Glomerular is a capillary that filters out protein-free plasma into tubular components. Tubular components consist of bowman capsule, proximal tubules, henle ansa, distal tubules and koligentes ducts. The bowman capsule functions in collecting glomerular filtrate. The juxtaglomerular apparatus is a component of a combination of vascular or tubular (Sherwood, 2014).

In the kidney, there are three processes, namely glomerular filtration, tubular reabsorption, and tubular secretion. The first step in the formation of urine is glomerular filtration, the process by which blood flows through the glomerular, protein-free plasma filtered through the glomerular capillaries into the bowman capsule. Under normal circumstances, 20% of plasma entering the glomerular is filtered. Furthermore, the filtrate flows through the tubules, beneficial ingredients for the body are returned to the peritubular capillary plasma. Selective movement of materials from the inside of the tubule (tubular lumen) into the blood, this process is called tubular reabsorption. And the latter process is tubular secretion, ie selective removal of substances from the peritubular capillaries into the tubular lumen; and then removed from the body (urinary excretion) (Sherwood, 2014).
2.2.2. Hypertension and Chronic Renal Failure

Hypertension is a blood pressure (BP) elevated above normal blood pressure (140/90 mmHg). Blood pressure is formed from the interaction between blood flow and peripheral vascular resistance. Blood pressure increases and reaches a peak if the blood flow is rapid, for example when systole time, then decreases when blood flow decreases as in diastole (Kabo, 2010).

Epidemiological data suggest that elevated systolic blood pressure, and diastolic blood pressure increase cardiovascular events. The higher the blood pressure the higher the risk of coronary heart disease (CHD), heart failure, stroke or kidney failure. Therefore hypertension disease should be treated or controlled (Kabo, 2010). The two main factors that influence blood pressure rise, namely when cardiac output and peripheral vascular resistance are on the rise. A person who has long-standing hypertension or severe hypertension can cause complications of organ damage to the heart, brain, kidneys, eyes, and peripheral blood vessels. In the kidneys can cause chronic kidney disease until kidney failure (Gunawan, 2012).
Kidney failure is divided into two, namely acute kidney failure or commonly referred to as ARF and chronic renal failure or CRF. Chronic renal failure is a kidney that progresses progressively, irreversibly and slowly, usually lasting several years. Chronic renal failure occurs when the nephron state is not functioning permanently and also there is a decrease in GFR (Glomerular Filtration Rate). Conversely, acute renal failure is a rapid and sudden decline in renal function and tends to be reversible. Chronic renal failure is a renal function disorder in which the body’s ability fails in maintaining metabolism and fluid in which electrolyte balance can cause uremia (urea retention and other nitrogenous waste in the body).

a. Classification

Hypertension can be classified according to high blood pressure and based on its aetiology. Based on high blood pressure, a person is said to have hypertension when his blood pressure is >140/90 mmHg. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and treatment of High Blood Pressure (JNV VII) hypertension is divided into 4 categories namely:

**Table 2.1** Classification of hypertension based on high blood pressure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;120</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120-139</td>
</tr>
<tr>
<td>Hypertension stage 1</td>
<td>140-159</td>
</tr>
<tr>
<td>Hypertension stage 2</td>
<td>≥160</td>
</tr>
</tbody>
</table>

(Source: Chobanian, 2004)

Based on the aetiology, hypertension is divided into essential hypertension and secondary hypertension. Primary or idiopathic hypertension is unknown hypertension or hypertension that is not or without having a clear pathological underlying abnormality. There are more than 90% of cases caused by genetic and environmental factors. Secondary or renal
hypertension includes 5-10% of cases of hypertension. Secondary or renal hypertension is hypertension due to kidney disease, endocrine hypertension and renal vascular hypertension. Secondary hypertension has a detectable cause whereas primary hypertension has no detectable cause (Gunawan, 2012).

Chronic renal failure can be classified into 5 (five) stages based on the degree of disease, that is:

**Table 2.2** Classification CKD based on the degree of disease

<table>
<thead>
<tr>
<th>STADIUM</th>
<th>EXPLANATION</th>
<th>GFR (mL/minute/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild GFR decrease</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>A moderate decrease in GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>GFR weight reduction</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

(Source: National Kidney Foundation, 2002)

In the first stage it, generally shows normal kidney function, in the second stage renal function begins to decline, in the third stage there is renal insufficiency, the fourth stage is renal failure and the fifth stage is a terminal renal failure. In the first and second stages, they require rigorous monitoring to maintain kidney function, the third stage requires aggressive treatment to slow the deterioration of the disease and in the fourth and fifth stages requires special management by a nephrology specialist to avoid complications of chronic long-term renal failure (Kilstoff, 2010).

b. Aetiology

In the past, glomerulonephritis was the leading cause of chronic renal failure. However, today the more common aetiology is diabetic and hypertensive nephropathy. This may be a more effective prevention and treatment of glomerulonephritis or decreased mortality due to other diseases
with diabetes and hypertension. Hypertension can lead to chronic renal failure in the elderly (Syamsudin, 2011).

Based on the diagnosis of comorbidities in hemodialysis patients in Indonesia in 2011, as follows: diabetes mellitus 23%, hypertension 46%, 11% cardiovascular, 2% cerebrovascular, 2% gastrointestinal tract, other urinary diseases 3%, 1% tuberculosis, hepatitis B 2%, 2% hepatitis, 3% malignancy, and others 5%. The hypertension is the highest disease that became a disease accompanying hemodialysis patients in 2011. Hypertensive disease is a disease that can be part of chronic kidney failure (Indonesian Renal Registry (IRR), 2011).

According to IRR (Indonesian Renal Registry) in 2011 based on the etiologic diagnosis, the most common cause of chronic renal failure in hemodialysis patients in 2011 was in hypertensive renal disease with a percentage of 34%. With a description of the percentage and terminology as follows:
Table 2.3  Percentage of CKD causes in hemodialysis patients in 2011 based on the type of diagnosis and terminology.

<table>
<thead>
<tr>
<th>No</th>
<th>TYPES OF DIAGNOSIS</th>
<th>TERMINOLOGY</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Primary Glomerulopathy</td>
<td>Characterized by a swollen body, hypertension and circulatory dams, proteinuria, microscopic hematuria. Macroscopic with erythrocyte cylinder, without systemic disease or other renal diseases</td>
<td>14%</td>
</tr>
<tr>
<td>2</td>
<td>Diabetic Nephropathy</td>
<td>Marked with a history of DM (+), proteinuria, at the funduscopy there is a capillary microaneurysym, in the absence of any previous evidence of previous renal disease</td>
<td>27%</td>
</tr>
<tr>
<td>3</td>
<td>Lupus Nephropathy</td>
<td>In the presence of clinical features of SLE, urine laboratory results are persistent proteinuria, haematuria, active sedimentary abnormalities, rise in antinuclear titers (ANA) and DNA binding antibody (dsDNA)</td>
<td>1%</td>
</tr>
<tr>
<td>4</td>
<td>Hypertension Kidney Disease</td>
<td>The presence of a history of hypertension, characterized by proteinuria, microscopic hematuria, and the presence of other damaged organ targets, such as LVH / hypertensive heart disease, hypertensive retinopathy</td>
<td>34%</td>
</tr>
<tr>
<td>5</td>
<td>Polycystic Kidney</td>
<td>Characterized by renal enlargement on palpation with any or all symptoms: proteinuria, haematuria, recurrent UTI (Urinary tract infection), increased blood pressure and low back pain</td>
<td>1%</td>
</tr>
<tr>
<td>6</td>
<td>Uric Acid Nephropathy</td>
<td>A history of recurrent Arthritis Gout and UTI also recurs. Laboratory results of uric acid levels are usually &gt;13mg% in males and &gt;10mg% in females, there is proteinuria with/without haematuria without complaint</td>
<td>2%</td>
</tr>
<tr>
<td>7</td>
<td>Obstructive Nephropathy</td>
<td>There is a history of urinary tract obstruction in lithiasis, BPH, vesicoureteral reflux, Ca vesica urinaria, Ca prostate or Ca cervix. Characterized by recurrent UTI, hypertension and hydronephrosis</td>
<td>8%</td>
</tr>
<tr>
<td>8</td>
<td>Chronic Pyelonephritis / PNC</td>
<td>Characterized by asymptomatic proteinuria with/without haematuria, recurrent UTI, hypertension, ultrasound picture: both kidneys constrict</td>
<td>6%</td>
</tr>
<tr>
<td>9</td>
<td>Not known</td>
<td>No known cause</td>
<td>1%</td>
</tr>
<tr>
<td>10</td>
<td>Etc</td>
<td></td>
<td>6%</td>
</tr>
</tbody>
</table>

(Source: Indonesian Renal Registrasy (IRR), 2011)
c. Pathophysiology

Initially the disease of chronic renal failure depends on the underlying disease, but in subsequent development the process is more or less the same. The occurrence of chronic renal failure is due to decreased renal function, as well as the accumulation of proteins or end products from metabolism in the blood whereas normally the protein is excreted into the urine. The more protein deposits in the blood the more severe the symptoms (Smeltzer, 2001).

There are several factors that can increase the risk of kidney disorders. Initiation factors initiate kidney damage and can be modified through drug therapy. Initiation factors include diabetes mellitus, hypertension, autoimmune disease, polycystic kidney disease, and drug toxicity. Furthermore, progressive factors that can accelerate the decline in kidney function after initiation of renal failure, and such factors are glycemia in diabetes, hypertension, proteinuria, and smoking (Wells, et al., 2009).

The occurrence of chronic renal failure starts from the loss of renal reserve where glomerular filtration rate is still normal or increased. Subsequently, a progressive but steady decrease in the function of the nephrons, with marked increases in serum urea and creatinine levels. Up to 60% glomerular filtration rate, the patient still has no (asymptomatic) complaints, but the urea and serum creatinine levels are elevated. At 30% glomerular filtration rate begins the occurrence of complaints such as, nocturia, weak body, nausea, poor appetite and weight loss. At glomerular filtration rates below 30%, symptoms and signs of uremia begin to look like, anemia, elevated blood pressure, impaired metabolism of phosphorus and calcium, pruritus (itching), nausea, vomiting, and others. At a glomerular filtration rate below 15% there will be more serious symptoms and complications and require renal replacement therapy, such as dialysis or renal transplantation. Thus, in such circumstances it is said to be the stages of renal failure (Suwitra, 2007).
Renal clearance or decreased clearance results from an increase in the number of glomerular that is not working so that it can cause kidney failure. With a decrease in glomerular filtration, creatinine clearance will decrease so that serum creatinine levels will increase. Furthermore, BUN (Blood Urea Nitrogen) or blood urea nitrogen levels will increase (Smeltzer, 2001).

Destruction of the nephron (glomerular and tubules)  
↓  
Decreased GFR (Glomerular Filtration Rate)  
↓  
The load of the dissolved material is greater than the reabsorbed  
↓  
Osmotic diuresis (abnormalities in producing urine)  
↓  
Damage of nephron → oliguria (urine production is small)  
↓  
Kretinin clearance up to 15 ml / min → kidney function lost 80% -90%  
↓  
Chronic renal failure

Figure 2.3 Pathophysiology of chronic renal failure  
(Source: Price dan Wilson, 2005)

d. Clinical Manifestations

The severity of signs and symptoms in patients with chronic renal failure depends on the part and extent of renal impairment, other underlying conditions and patient age. Cardiovascular and pulmonary disorders, the occurrence of congestive heart failure and pulmonary oedema can be caused by excess fluid and salt, due to excess fluid and Na⁺ may also cause hypertension in patients with chronic renal failure, and pericarditis due to irritation of the pericardial layer by the uremic toxin (Smeltzer, 2001).

Hematologic abnormalities in patients with chronic renal failure occur in red blood cells, white blood cell function, and blood clotting parameters. The disease commonly found in these disorders is normochromic normocytic anaemia caused by lack of erythropoietin production and loss
of stimulatory effects on erythropoiesis. In chronic renal failure patients, hemostasis abnormalities can lead to bruising manifestations, increased bleeding during surgery, and increased spontaneous bleeding in the gastrointestinal and cerebrovascular tract (Ganong, 2010).

Neuromuscular abnormalities include being unable to concentrate, muscle twitching, and seizures (Smeltzer, 2001). Gastrointestinal (GI) abnormalities, patients with uremia 25% have peptic ulcer disease. Another disorder is gastroenteritis, a uremic characterized by a mucosal ulcer accompanied by expulsion of blood in chronic renal failure patients, and a distinctive breath odour (uremic fetor) resulting from the decomposition of urea into ammonia by enzymes in saliva (Ganong, 2010).

Skin disorders in patients with chronic renal failure is indicated by skin which appears pale from anaemia, discolouration of the skin to grey due to transfusion-associated hemochromatosis, ecchymoses and hematoma due to clotting, pruritus and excoriation caused by Ca\(^{2+}\) deposition by secondary hyperparathyroidism. If the concentration of urea is high, the evaporation of the sweat leaves the rest of the urea commonly called uremic frost (Ganong, 2010).
Table 2.4 Manifestation of CKD

<table>
<thead>
<tr>
<th>Liquid and Electrolyte</th>
<th>Cardiovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Expansion &amp; contraction of the volume</td>
<td>• Arterial hypertension</td>
</tr>
<tr>
<td>• Hypernatremia and hyponatremia</td>
<td>• Congestive heart failure or pulmonary oedema</td>
</tr>
<tr>
<td>• Hyperkalemia and hypokalemia</td>
<td>• Pericarditis</td>
</tr>
<tr>
<td>• Metabolic acidosis</td>
<td>• Cardiomyopathy</td>
</tr>
<tr>
<td>• Hypocalcemia</td>
<td>• Uremic lung</td>
</tr>
<tr>
<td><strong>Bones and Minerals</strong></td>
<td></td>
</tr>
<tr>
<td>• Kidney Osteodystrophy</td>
<td>• Acceleration of atherosclerosis</td>
</tr>
<tr>
<td>• Osteomalacia</td>
<td>• Hypotension and arrhythmia</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td></td>
</tr>
<tr>
<td>• Carbohydrate intolerance</td>
<td>• Pale skin</td>
</tr>
<tr>
<td>• Hypothermia</td>
<td>• Hyperpigmentation</td>
</tr>
<tr>
<td>• Hypertriglyceridaemia</td>
<td>• Pruritus</td>
</tr>
<tr>
<td>• Protein-calorie malnutrition</td>
<td>• Ecchymoses</td>
</tr>
<tr>
<td>• Disturbance grows</td>
<td>• Uremic</td>
</tr>
<tr>
<td>• Sexual infertility and dysfunction</td>
<td></td>
</tr>
<tr>
<td>• Amenorrhoe</td>
<td>• Anorexia</td>
</tr>
<tr>
<td>• Dialysis arthropathy</td>
<td>• Nausea and vomiting</td>
</tr>
<tr>
<td><strong>Neuromuscular</strong></td>
<td>• Uremic fetor</td>
</tr>
<tr>
<td>• Fatigue</td>
<td>• Gastroenteritis</td>
</tr>
<tr>
<td>• Sleep disturbance</td>
<td>• Peptic ulcer</td>
</tr>
<tr>
<td>• Mental disorders</td>
<td>• Gastrointestinal haemorrhage</td>
</tr>
<tr>
<td>• Lethargy</td>
<td>• Hepatitis</td>
</tr>
<tr>
<td>• Asterixis</td>
<td>• Refractory ascites in hemodialysis</td>
</tr>
<tr>
<td>• Muscle injuries</td>
<td>• Peritonitis</td>
</tr>
<tr>
<td>• Peripheral neuropathy</td>
<td></td>
</tr>
<tr>
<td>• Restless leg syndrome</td>
<td>• Normochromic normocytic anaemia</td>
</tr>
<tr>
<td>• Paralysis</td>
<td>• Microcytic anaemia</td>
</tr>
<tr>
<td>• Myoclonus</td>
<td>• Lymphocytopenia</td>
</tr>
<tr>
<td>• Seizures</td>
<td>• Diathesis of bleeding</td>
</tr>
<tr>
<td>• Coma</td>
<td>• Increased susceptibility to infection</td>
</tr>
<tr>
<td>• Muscle cramps</td>
<td>• Splenomegaly and hypersplenism</td>
</tr>
<tr>
<td>• Dialysis imbalance syndrome</td>
<td>• Leukopenia</td>
</tr>
<tr>
<td>• Dialysis density</td>
<td>• Hypocomplementemia</td>
</tr>
<tr>
<td>• Myopathy</td>
<td></td>
</tr>
</tbody>
</table>

(Source: Ganong, 2010)
2.2.3. Hemodialysis

Dialysis is a process whereby fluids and waste products are removed from the body when the kidneys are no longer able to perform the process. This dialysis aims to maintain the patient’s life until the kidney function undergoes recovery. Patients with chronic renal failure are in need of renal replacement therapy and one of them is therapy with blood washing or hemodialysis. Hemodialysis is one type of replacement therapy in patients with chronic renal failure. The hemodialysis process generally takes 4-5 hours every 2 times a week (Tjay and Rahardja, 2007).

Hemodialysis is a therapy used for patients with chronic renal failure in preventing death but this hemodialysis therapy is not to cure or recover kidney disease. Patients require chronic dialysis therapy when maintaining their survival and control uremic symptoms (Smeltzer, 2001).

The hemodialysis process is performed by draining blood into an artificial kidney tube or dialyser which consists of two separate compartments, containing thousands of fine cellophane tubules that act as semipermeable membranes. Then the patient’s blood is pumped and then fed to a blood compartment bounded by an artificial or artificial semipermeable membrane with a dialysate compartment. The dialysate compartment is permeated with pyrogen-free dialysis. Separate dialysis and blood fluids will change in concentration because the solute is moving from high concentration to low concentration (Suwitra, 2007).

There are three principles underlying the work of hemodialysis, namely diffusion, osmosis and ultrafiltration. Toxins and waste substances present in the blood are excreted through the diffusion process from high concentrations of blood into the low concentration of dialysate fluid. So that toxins and waste substances can be excreted through diesis. Excessive water excretes from the body through the osmosis process (Smeltzer, 2001).
The discharge of water can be controlled by a pressure gradient in which water moves from a higher pressure region (the patient’s body) to a lower pressure (dialysate fluid). This gradient can be increased by the added negative pressure commonly referred to as ultrafiltration in a dialysis machine. This pressure is utilized as a suction force on the membrane and facilitates water expenditure. Because the patient cannot excrete water, this strength is needed to remove fluid until the fluid or isovolemia balance is reached (Smeltzer, 2001).

There are three main components in the hemodialysis process namely the blood compartment, the washing liquid compartment (dialysate), and the artificial kidney (dialyser). Blood is removed from the arterial blood vessels, then into the dialyser machine by pumping process. There was dialysis (the process of purifying the blood in dialysers), then the cleaned blood went into the veins (Price and Wilson, 2005).

Figure 2.4 Hemodialysis process

(Source: Smeltzer, 2001)
2.2.4. Management of Antihypertensive Therapy

According to JNC VII treatment of hypertension aims to reduce mortality and morbidity in renal and cardiovascular patients. The main goal in the management of hypertension is the achievement of systolic pressure <140/90 mmHg. In patients with hypertension or kidney disease, the blood pressure is <130/80 mmHg. Treatment of antihypertensive treatment in chronic renal failure with hemodialysis which aims to improve the quality of patients life, minimize the patient’s plight and slow the development of chronic renal failure. Management of antihypertensive therapy is divided into two, namely non-pharmacological therapy and pharmacological therapy (Chobanian, 2004).

According to JNC VIII, the target of systolic blood pressure in patients aged 60 years and over to <150 mmHg and blood pressure target patients with chronic renal failure with various ages and different types of the race with or without diabetes is changed to <140/90 mmHg. At the age of 18≥ years with chronic kidney disease, antihypertensive therapy should be with ACE-I or ARB to improve the outcome of the kidney. It is for all patients with chronic kidney disease with hypertension regardless of race or diabetes status (Muhadi, 2016).

a. Non Pharmacological Therapy

Nonpharmacologic therapy in prehypertensive and hypertensive patients should be to modify lifestyle such as weight loss if overweight (Sukandar, 2013). Maintain normal body weight of Body Mass Index (BMI) 18.5-24.9 kg / m2); consume a diet rich in fruits, vegetables, and low-fat dairy products to reduce total saturated fat and body fat; reducing sodium intake to no more than 100 mmol per day (2.4 g sodium / day or 6 g / day NaCl); low protein diet (0.6 to 0.75 g / kg / day) to slow the progression of chronic renal failure; performing mild aerobic physical activity on a regular basis, such as walking (at least 30 minutes per day, almost every day of the week); avoid alcohol consumption; as well as to stop smoking if the patient
is a smoker (Chobanian, 2004).

b. Pharmacological Therapy

Treatment of pharmacological therapy for patients with chronic renal failure with hemodialysis include using antihypertensive drugs because most antihypertensive drugs can lower blood pressure by decreasing cardiac output and decreasing peripheral resistance (Harvey and Champe, 2013).

Types of antihypertensive drugs have 5 groups of drugs called first-line drugs or commonly referred to as first-line drugs, where these antihypertensive drugs are commonly used for early treatment of hypertension namely; diuretics, adrenergic beta-receptor blockers (β-blockers); angiotensin-converting enzyme inhibitors (ACE-inhibitors); angiotensin receptor blocker (angiotensin receptor blocker, ARB); and calcium antagonists (Gunawan, 2012). Of the several types of antihypertensive drugs for chronic renal failure, ACE-Inhibitor and ARB drugs can lower blood pressure and can reduce intraglomerular pressure (Sukandara, 2013). It can also reduce proteinuria even slow the development of chronic renal failure (Price and Wilson, 2005).

Diuretics are drugs that work to increase the excretion of sodium, water and chloride thereby decreasing blood volume and extracellular fluid levels so there was cardiac output and blood pressure dropped. Therefore, this diuretic drug can lower blood pressure. Diuretic drugs commonly used as antihypertensive drugs include thiazide diuretics, potassium-sparing diuretics, and strong diuretics (loop diuretics) (Gunawan, 2012).

Thiazide diuretic drug class is the main choice for hypertensive drug so it is used as an initial therapy for high blood pressure sufferers used as a single drug or in combination with other class of antihypertensive drugs (Tjay & Rahardja, 2007). Among the reasons thiazide group medications are often combined with other antihypertensive drugs because they can increase the effectiveness of other antihypertensives by different mechanisms of
action so that the dosage can be reduced and can also prevent fluid retention by other antihypertensives so that the effects of these drugs can survive (Gunawan, 2012).

The thiazide group is generally less effective in impaired renal function, as it can worsen renal function and in prolonged use will lead to hyperlipidemia (elevated cholesterol, LDL, and triglycerides) (Gunawan, 2012). However, thiazides are effectively used for patients with renal impairment function with glomerular filtration rate above 30 mL/min, and thiazides are also very effective for lowering blood pressure. It can also be used to overcome the effects of increased volume and sodium. Meanwhile, side effects are caused by hypokalemia, hypercalcemia, and hyperuricemia (Fakhrunnisa, 2016).

Thiazide diuretic drug class is a drug that inhibits transport with Na-Cl in the distal renal tubule, so that the excretion of Na⁺ and Cl⁻ increases. There are several thiazides including hydrochlorothiazide (HCT), bendroflumethiazide, indapamide, chlorothiazide, and others (Gunawan, 2012). HCT is used in small doses of 12.5-25 mg/day. With this, it can lower blood pressure, reduce morbidity and mortality, not cause side effects, so HCT with this small dose is recommended for first-line antihypertensive drugs (Kabo, 2010).

Indapamide (thiazide diuretic class) is a drug that has effectiveness in renal dysfunction patients because it is neutral in fat metabolism and effectively pervert ventricular hypertrophy (Gunawan, 2013). These drugs include non-diuretic thiazide diuretics. These drugs lower blood pressure without increasing urine production. The advantage is that it can lower SBP (Systolic Blood Pressure) without affecting DBP (Diastolic Blood Pressure) (Kabo, 2010).

Thiazide diuretic drugs have antagonism with non-steroidal anti-inflammatory drugs (AINS), especially indomethacin because NSAIDs can
inhibit prostaglandin synthesis which plays a role in regulating renal blood flow and transport of water and salt. As a result, sodium and water retention will reduce the effects of almost all antihypertensive drugs. Side effects of high-dose thiazide diuretic medications cause hypokalemia, hyponatremia, hypomagnesemia, hypercalcemia, and may inhibit uric acid excretion of the kidneys (Gunawan, 2012).

Loop diuretics work in henle ascending as thick epithelial portions by inhibiting cotransport $\text{Na}^+$, $\text{K}$, $\text{Cl}^-$ and inhibiting the reabsorption of water and electrolytes. Loop diuretics can be used as antihypertensive and oedema drugs, and are more often selected for chronic renal failure patients with GFR less than $30 \text{ ml/min} / 1.73 \text{ m}^2$ (Wells, et al., 2009). Loop diuretics are commonly used to reduce lung oedema in patients with congestive heart failure because of the potential and the way it works more rapidly and the diuretic effect is stronger than the thiazide group. Therefore loop diuretics are rarely used as antihypertensives, except in patients with impaired renal function (creatinine serum $> 2.5 \text{ mg/dL}$) or heart failure (Gunawan, 2012).

This loop diuretic drug has a major side effect which can cause hypokalemia. This loop diuretic is more potent than thiazide diuretics because loop diuretics are the preferred type of diuretic for patients whose low glomerular filtration rates are low. In addition, these loop diuretics can increase the toxicity of the drug so that it can eventually cause ear damage (ototoxicity) also in the kidney (nephrotoxicity) (Stringer, 2008).

Amiloride, spironolactone and triamterene are types of potassium-sparing diuretic drugs. Its use with a combination of other diuretics are able to prevent hypokalemia. Potassium-sparing diuretics are often used in combination with other types of diuretics to help maintaining potassium balance since potassium-sparing diuretics can cause hyperkalemia (Stringer, 2008). Potassium-sparing diuretics’s effect is very weak if used singly. This diuretic can be used to treat patients with potassium deficiency as well as
sodium caused by other diuretic drugs (Fakhrunnisa, 2016). However, it can cause hyperkalemia when administered to patients with renal failure or when combined with ACE inhibitors, ARBs, β-blockers, NSAIDs or with potassium supplements. When serum creatinine is more than 2.5 mg / dL the use of potassium-sparing diuretics should also be avoided (Gunawan, 2012).

![Figure 2.5](https://example.com/figure2.5.png)

**Figure 2.5** Mechanisms and work location of diuretic drugs

(Source: Harvey dan Champe, 2013)

β inhibitors are recommended as first-line therapy (Harvey and Champe, 2013). Antihypertensive mechanisms on β-blocker administration, namely: decreased heart rate and myocardial contractility resulting in decreased cardiac output; barriers to renin secretion in renal juxtaglomerular cells resulting from decreased angiotensin II production; a central effect affecting sympathetic nervous activity. β-blockers are usually used as first-stage drugs in mild to moderate hypertension especially in patients with coronary heart disease (especially after acute myocardial infarction), supraventricular and ventricular arrhythmias without conduction abnormalities, also in hyperdynamic young patients (Gunawan, 2012).
β-blockers can lower blood pressure especially it can decrease cardiac output. It can also decrease sympathetic outflow from the sympathetic nervous system and inhibit the release of renin from the kidneys so as to decrease the formation of angiotensin II and aldosterone secretion (Harvey and Champe, 2013). The β-blocker drugs include propranolol, metoprolol, nadolol, carteolol, atenolol, betaxolol, bisoprolol, pindolol, acebutolol, penbutolol, labetalol, carvedilol, and esmolol. Side effects of β-blocking drugs can cause bradycardia and sympathetic nervous system side effects such as fatigue, insomnia, and hallucinations. It can also cause hypotension. Sudden drug withdrawal may induce angina, myocardial infarction, even sudden death in ischemic heart patients (Gunawan, 2012).

![Image of the mechanism of action of the adrenoceptor-β inhibitor](Source: Harvey and Champe, 2013)

α-adrenoceptor inhibitors are drugs used for mild to moderate hypertension when diuretics and β-blockers are less effective; although not the first-choice drug (Tjay and Rahardja, 2015). The antihypertensive mechanism in α-blockers, alpha-1 receptor blockage leads to vasodilation in arterioles and venules thereby decreasing peripheral resistance. Venodilation also causes the reduced venous to return to decrease cardiac output. α-blockers have advantages such as positive effects on blood lipids (lowers LDL and triglycerides also increases HDL), reduces insulin resistance so it is suitable for hypertensive patients with dyslipidemia and diabetes mellitus.
It also improves peripheral vascular insufficiency, does not interfere with heart function, does not interfere with renal blood flow and does not interact with NSAIDs (Gunawan, 2012). The side effects of α-blocker drugs include orthostatic hypotension in early dosing or when dose increases (first dose phenomenon). These side effects can be avoided by starting low doses and gradually increasing them. Other side effects include dizziness, headache, nasal congestion, sleep disturbances, oedema, and heart pounding (Tjay and Rahardja, 2015).

Antiadrenergic central work is one of the drugs for hypertensive patients, and the most commonly used in this class is methyldopa and clonidine. Methyldopa is a second-line antihypertensive drug. This drug is effective when consumed by combining diuretics. However, its users are limited by the frequent side effects. The effective dose of methyldopa at least 2 x 125 mg/day and maximum dose of 3 g/day. And for post-surgical hypertension is often given intravenously with an intermittent infusion of 250-1000 mg every 6 hours (Gunawan, 2012).

Clonidine is a drug used for the treatment of hypertension. Clonidine does not decrease renal blood flow or glomerular filtration so useful in the treatment of hypertension with complications of kidney disease (Harvey and Champe, 2013). Oral clonidine absorption is rapid and complete with a bioavailability of 95%. Clonidine is not only given for oral alone but can be administered transdermally with plasma levels equivalent to oral administration. 50% of clonidine is eliminated intact through urine. Plasma levels increase in kidney function disorder or in the elderly. For side effects of this drug are dry mouth, sedation, dizziness, nausea, orthostatic symptoms when the fluid depletion. Fluid retention and pseudo-tolerance occur when clonidine is used as a single drug (Gunawan, 2012).

Vasodilator drugs are potent drugs, especially when combined with β-blockers and thiazides. And also must be careful in case of danger of a very
rapid drop in blood pressure (BPOM, 2008). Drugs classified as vasodilators are hydralazine, minoxidil, and diazoxide. Hydralazine is a drug used to treat moderate to severe hypertension. These drugs are almost always combined with β-blockers, such as propranolol (to balance reflex tachycardia), and diuretics (to decrease urinary retention). Hydralazine monotherapy is used to control blood pressure in pregnancy-induced hypertension (Harvey and Champe, 2013). Hydralazine is well absorbed through the gastrointestinal tract, but due to the presence of a large first cross metabolism, the hydralazine bioavailability is relatively low (Goodman and Gilman, 2010). Hydralazine can cause headaches, nausea, tachycardia, angina pectoris, palpitations. And this drug is contraindicated in hypertension with CHD is also not recommended for patients aged over 40 years (Gunawan, 2012).

Angiotensin Converting Enzyme (ACE) is an enzyme that converts angiotensin I into angiotensin II which has a very strong vasoconstriction effect and stimulates aldosterone secretion from the adrenal cortex. ACE also plays a role in the degradation of bradykinin into non-active quinine. Bradykinin is a vasodilator that works by increasing the synthesis of EDRF (endothelium-derived relaxing factor) and prostacyclin (PGI2) in vascular endothelial cells (Gunawan, 2012).

Captopril is a class of ACE-Inhibitor drugs widely used for the treatment of hypertension and heart failure. ACE-Inhibitors inhibit angiotensin I conversion to angiotensin II resulting in vasodilation and decreased aldosterone secretion. And also occurs inhibition of bradykinin degradation so that bradykinin levels in the blood increases and acts as a vasodilation effect of ACE-Inhibitor. In the kidneys, ACE-Inhibitors cause vasodilation of the renal artery in order to increase renal blood flow and improve glomerular filtration rate. ACE-Inhibitors elicit more dominant vasodilation in efferent arterioles than afferent arterioles in order to decrease intraglomerular pressure. This effect can reduce proteinuria in diabetic nephropathy and nephrotic syndrome. It can also slow the progression of
diabetic nephropathy (Gunawan, 2012).

Giving to pregnant women there is a contraindication to this class of ACE-Inhibitor drugs because they are teratogenic. Also administered to breastfeeding mothers as ACE-Inhibitors are excreted through breast milk and adversely affect infant renal function. While ACE-Inhibitor is indicated for hypertension in chronic kidney disease. However, care should be taken when hyperkalemia patients, because ACE-Inhibitor will aggravate hyperkalemia (Wells, et al., 2009).

ARB (Angiotensin Receptor Blocker) is a class of drugs that inhibit all effects of angiotensin II, such as vasoconstriction, aldosterone secretion, sympathetic nerve stimulation, central effects of angiotensin II. This ARB class drug has an effect similar to that of ACE-Inhibitor. However, since it does not affect the metabolism of bradykinin then this class of drugs has no side effects of a dry cough and angioedema as occurs in ACE-Inhibitors. ARB is very effective in lowering blood pressure in hypertensive patients with high levels of renin but is less effective in hypertension with low renin activity. Thus, in hypovolemia patients, the ARB dose should be lowered (Gunawan, 2012).

Figure 2.7 Effect of ACE-Inhibitor drug
(Source: Harvey dan Champe, 2013)
Calcium antagonists inhibit calcium influx in smooth muscle cells of the blood vessels and myocardium. The calcium antagonist is one of the first classes of antihypertensive drugs. Calcium antagonists have been shown to be very effective in hypertension with low levels of renin as in elderly. Can be combined with ACE-Inhibitor class drugs, methyldopa or β-blockers. However, when combined with β-blockers, a vasculoselective (dihydropyridine) antagonist should be selected (Gunawan, 2012).

The mechanism of action of this calcium antagonist drug by inhibiting the entry of calcium into the cells through the L-channel. Calcium antagonists are divided into two major classes, namely non-dihydropyridine calcium antagonists (phenylalkylamine class and benzodiazepine) and dihydropyridine calcium antagonists (1,4-dihydropyridine). The dihydropyridine group primarily acts on the arteries to function as an antihypertensive drug, while the non-dihydropyridine group affects the cardiac conduction system and tends to slow the heart rate, its hypertensive effects through peripheral vasodilation and decreased peripheral resistance (Lucky, 2007).

According to Pharmacotherapy Handbook 7th edition of 2009, management of pharmacological therapy in hypertensive patients can be described on the hypertension therapy algorithm as follows:
Obat Pilihan

No Compelling Indication

Hypertension Stage 1
SBP 140-159 or DBP 90-99 mm Hg

Thiazide-type diuretics: ACE-I, ARB, CCB atau kombinasi

Left Ventricular Function

Diuretika with ACE-I

Than add β-blocker

ARB or aldosterone antagonist

Compelling Indication

Hypertension Stage 2
SBP >160 or DBP ≥100 mmHg

Two-drug combination: Usually a thiazide-type diuretic with an ACEI, or ARB, or CCB

Postmyocardial Infarction

β-blocker; than add ACE-I or ARB

Aldosterone antagonist

β-blocker; than add ACE-I or ARB

CCB, Diuretic

Coronary Disease

Diabetes Mellitus

ACE-I or ARB

β-blocker

CKD

ACE-I or ARB

Recurrent Stroke Prevention

Diuretic & ACE-I or ARB

Figure 2.8 Algorithm for treatment of hypertension

(Source: Wells, et al., 2009)
Management of pharmacological therapy in patients hypertension with chronic renal failure can be described by the following algorithm:

1. **Step 1**
   - Start ACE-I or ARB
   - Recheck $S_{cr}$ and $K^+$ in 1 week, if $S_{cr}$ or $K^+$ ↑ > 30%, discontinue agent.
   - BP still not at goal ($<130/80$ mmHg or $<125/75$ mmHg for patients with proteinuria)

2. **Step 2**
   - Add diuretic
   - If $Cl_{cr}$ ≥ 30 ml/min, add thiazide diuretic
   - If $Cl_{cr}$ < 30 ml/min, add loop diuretic
   - BP still not at goal

3. **Step 3**
   - Add long-acting CCB. May also consider adding low-dose $\beta$-blocker instead of CCB at this time if patient has angina, heart failure, or arrhythmia necessitating their use
   - BP still not at goal
   - Baseline pulse ≥ 84
   - Baseline pulse < 84

4. **Step 4**
   - Add low-dose $\beta$-blocker or $\alpha/\beta$-blocker (if not already being used).
   - NOTE: the use of a $\beta$ blocker and a nondihydropyridine CCB should be avoided in the elderly and those with conduction abnormalities

5. **Step 5**
   - Add long-acting $\alpha$-blocker, central $\alpha$-agonis, or vasodilator.
   - NOTE: central $\alpha$-agonis (ex: clonidine) should not be used with $\beta$-blocker due to the high likelihood of severe bradycardia

![Figure 2.9 Hypertension management algorithm for patients with chronic kidney disease](Source: Wells, et al., 2009)
2.3. Conceptual Framework

Chronic renal failure patients with hypertension undergoing hemodialysis

Blood pressure > 140/90 mmHg

Treatment of antihypertensive drugs

Evaluate the use of antihypertensive drugs

Right patient

The exact medicine

The exact dose

CHAPTER 3
RESEARCH METHODS

3.1. Time and Place of Execution

The timing of medical record data in chronic renal failure outpatients with hemodialysis started from November 2017 to January 2018 at RSUP dr. Soeradji Tirtonegoro Klaten.

3.2. Research Design

This research is a non-experimental observational descriptive research. The data used in this study is retrospective data by performing medical record data of chronic renal failure outpatient with hemodialysis at dr. Soeradji Tirtonegoro Klaten in 2017.

3.3. Operational Definition

1. Descriptive research is a study that describes the phenomenon found as it is, it does not analyze how and why the phenomenon may occur nor does it require a hypothesis.
2. Appropriate Patient is accurate in the administration of drugs that are in accordance with the patient’s condition or history of the patient’s illness.
3. Precise Medication is the precision in the selection of drugs in accordance with its drug of choice, which is used safely for outpatients with chronic renal failure who undergo hemodialysis.
4. Precise Dosage is the precision in administering the appropriate dose of medication to outpatients with chronic renal failure who undergo hemodialysis.
5. Chronic Kidney Failure is an outpatient diagnosed with chronic renal failure with hypertension.
6. Antihypertensive drugs are drugs used for the treatment of hypertension in outpatients with chronic renal failure with hemodialysis.
3.4. Population and Number of Samples

The population used for this study were all outpatients who were diagnosed with chronic renal failure with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten in 2017. The sample used in this study were all outpatients diagnosed with chronic renal failure with hemodialysis and patients who received antihypertensive treatment therapy in RSUP dr. Soeradji Tirtonegoro Klaten in 2017, with the following sample criteria:

a. Inclusion criteria
1. Patients diagnosed with chronic renal failure with hypertension undergoing hemodialysis
2. Patients with blood pressure >140/90 mmHg
3. Patients receiving antihypertensive medications
4. Patients who underwent outpatient in RSUP dr. Soeradji Tirtonegoro Klaten in 2017
5. Complete patient data

b. Exclusion criteria
1. Incomplete patient data
2. Unrecognized medical record
3. Patients who are not receiving antihypertensive therapy
4. Patients with CKD without hypertension
5. Patients with blood pressure <140/90 mmHg

3.5. Research Phase

1. Research permits

Permission of this research was granted by submitting a research permit from the Pharmacy Program of Universitas Darussalam Gontor to the director of RSUP dr. Soeradji Tirtonegoro Klaten with the endorsed research proposal.
2. Observation

Observation is done by recording the patient’s medical record number by knowing the number of chronic renal failure patients with hemodialysis who underwent outpatient at RSUP dr. Soeradjji Tirtonegoro Klaten in 2017.

3. Data collection

Data were obtained from medical records data collection in patients with chronic renal failure with hemodialysis who underwent outpatient in RSUP dr. Soeradjji Tirtonegoro Klaten in 2017 and who received antihypertensive treatment. The data obtained thus were then evaluated for their rationale in the treatment of antihypertensive in patients with chronic renal failure with hemodialysis seen from the exact aspect of the drug, the exact patient, and the exact dosage; then the data is analyzed descriptively.

3.6. Data Analysis

Evaluation of the use of antihypertensive drugs includes drug accuracy, patient accuracy, and accuracy of dosage. The evaluation was performed by comparing drug usage data in each outpatient of chronic renal failure who received antihypertensive therapy with the standard of study used. The data obtained is then processed into percentages and presented in tabular form.

Data analysis in this research is non-experimental descriptive. The data obtained include medical record number, patient name, age, sex, primary and accompanying diagnoses, physical examination, drug administration data (drug name, dosage, and frequency of administration). They are grouped by their respective distributions, into percentages and presented in tabular form. Then they are analyzed by descriptive analysis method.

The exact percentage of patients is the number of prescribed antihypertensive drugs corresponding to the condition of chronic renal failure patients with hemodialysis outpatients divided by all prescribed or
given antihypertensive prescriptions and then multiplied by 100%.

\[ \text{The exact percentage of patients} = \frac{\text{the amount of patient accuracy}}{\text{all antihypertensives used}} \times 100\% \]

The appropriate percentage of a drug is the number of prescribed effective antihypertensive drugs for outpatients who have a chronic renal failure with hemodialysis divided by all prescribed or given antihypertensive prescriptions, and then multiplied by 100%.

\[ \text{The appropriate percentage of drug} = \frac{\text{number of effective antihypertensive drugs}}{\text{all antihypertensives used}} \times 100\% \]

The exact percentage of dosage is the number of accurate doses of antihypertensive drugs appropriate to the condition of chronic renal failure patients with hemodialysis outpatient divided by all prescribed antihypertensives used or given and then multiplied by 100%.

\[ \text{The exact percentage doses} = \frac{\text{the amount of accuracy of the antihypertensive dose}}{\text{all antihypertensives used}} \times 100\% \]
CHAPTER 4
RESULTS AND DISCUSSION

4.1. Description of Research Data

Diseases that are familiar and often found in the world of health is hypertension. In the 4th report of the Indonesian Renal Registry (IRR) it states that hypertension is the highest disease that became a disease accompanying hemodialysis patients in 2011. The hypertension disease is a disease that can be part of chronic kidney failure (IRR, 2011).

Provision of antihypertensive drugs is very important in patients who have a hypertension disease with renal failure undergoing hemodialysis. Hypertension can accelerate the progression of the disease and increase the mortality rate of patients with renal failure who undergo hemodialysis. Thus, it can be concluded how important the provision of antihypertensive drugs in patients with hemodialysis with these conditions (National Kidney Foundation, 2002). Analyzing antihypertensive drugs is necessary to prevent the onset of new diseases or the occurrence of disease complications; which can be seen in terms of patient accuracy, drug accuracy, and accuracy of dosage.

This research was conducted at dr. Soeradji Tirtonegoro Klaten from 8th of November 2017, to 2nd of January 2018. Data were obtained from medical records which were outpatients receiving treatment of hypertension with chronic renal failure undergoing hemodialysis. The patient sample was taken according to the inclusion criteria of this study and the sampling used purposive sampling method. Purposive sampling is a method of intentional sampling with sample requirements that have been determined by researchers. Data were collected retrospectively. Then the data on the treatment of hypertension were evaluated based on patient accuracy, drug and dosage in outpatient of chronic renal failure who underwent hemodialysis.
The data were analyzed using non experimental/descriptive adapted from the reference book Drug Dosing Renal Failure, British National Formulary 68, Drug Information Handbook 17th edition, KDOQI National Kidney Foundation, Joint National Committee of Eight Report 2013, Pharmacotherapy Handbook 9th edition and American Society of Hypertension. In this study, the results were obtained from a population of 243 patients with chronic renal failure with hemodialysis. The samples which meet the inclusion criteria were 55 patients and the exclusion criteria were 188 patients.

There were 188 samples of patients who were included in the exclusion criteria or samples who did not meet the inclusion criteria in this study. This happened these 188 patients had blood pressure <140/90 mmHg,
incomplete patient data, unreadable medical records, were non-outpatient patients, patients who did not receive antihypertensive therapy, non-hemodialysis CKD patients and patients with CKD without hypertension. While in this study the sample used is in accordance with inclusion criteria.

4.2. Distribution of Patients by Sex and Age

4.2.1. By Sex

Based on sex this study obtained the most results in male compared with female. Male have the largest number of 35 patients with a percentage of 64% while female of 20 patients have a percentage of 36%.

**Table 4.1** Distribution of patients by sex in outpatients chronic renal failure with hemodialysis in RSUP dr. Soeradjı Tirtonegoro Klaten 2017.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Amount</th>
<th>(%) Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>35</td>
<td>64%</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>36%</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100%</td>
</tr>
</tbody>
</table>

(Source: Data of research result)

This is similar to previous research in Anita Salwa’s study (2013) which showed that male patient have more hypertensive patients. In males, there were 29 patients (58%) and 21 women (42%) of 50 cases (Salwa, 2013). According to the Central Java Provincial Health Office in 2015, the health profile of Central Java Province reported that people with high blood pressure or hypertension by sex, the percentage of hypertension in males is 20,88%, higher than female which is 16,28 % (Dinkes, 2015).

The incidence of hypertension occurs more frequently in middle-aged male patients than in middle-aged women. As we get older and obese, the prevalence of hypertension can increase (Harvey and Champe, 2013). One of the reasons why many men are affected by chronic renal failure
is that many men have a smoking habit. Prasetyo study results stated that 14 respondents (60.9%) of men with productive age have hypertension because some of them have the habit of smoking 1/2 to 1 pack per day. Smoking habits make the heart work harder so it can encourage the rise in blood pressure (Prasetyo, 2014).

In the Malaeny study, et al. (2017) stated that smoking can cause increased cholesterol in the blood because smoking can increase LDL levels and decrease HDL levels in the blood leading to atherosclerosis. Then the heart work is getting heavier (Malaeny, et al., 2017). Apparently, there is a relationship between smoking habits with the incidence of hypertension. The results of Setyanda et al., Stated that with the chi-square test results, there was a correlation between smoking habit and hypertension disease (p = 0.003) (Setyanda, et al., 2015).

Lechner’s (2016) study shows that women have a higher body resistance to kidney damage compared to men. The 2-fructose-1, 6-bisphosphatase, and alpha-glutathione-S-transferase enzymes are renal cell enzymes. The researchers measured and found the enzyme in proximal tubules. When the proximal tubule is damaged, the enzyme is excreted into urine with a woman’s menstrual period (Lechner, 2016).

The result of basic health research in 2013 shows that the prevalence of chronic renal failure in male gender (0.3%) is higher than that of women (0.2%) (Kemenkes, 2013). Based on sex, in this study it can be concluded that outpatients with chronic renal failure with hypertension who undergo hemodialysis and get antihypertensive therapy at RSUP dr. Soeradji Tirtonegoro Klaten in 2017 obtained the greatest results in the male patients.

4.2.2. By Age

Grouping by age in outpatients with chronic renal failure with hemodialysis in RSUP dr. Soeradji Tirtonegoro Klaten 2017 can be seen in Table 4.2 below:
Table 4.2  The distribution of patients by age in outpatients chronic renal failure with hemodialysis in RSUP dr. Soeradj Tirtonegoro Klaten 2017.

<table>
<thead>
<tr>
<th>Age (th)</th>
<th>Amount</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-40</td>
<td>9</td>
<td>17%</td>
</tr>
<tr>
<td>41-75</td>
<td>42</td>
<td>76%</td>
</tr>
<tr>
<td>&gt;75</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>100%</td>
</tr>
</tbody>
</table>

(Source: Data of research result)

If grouped by age, the age range of 18-40 years is 9 patients (17%); 41-75 years old as many as 42 patients (76%); and age over 75 years as many as 4 patients (7%). The largest number in this study was in the 41-75 year age range of 42 patients (76%). As in Fakhrunnisa (2016) study, hypertensive patients with chronic renal failure who underwent hemodialysis accounted for 29 patients and had the greatest number in the 41-75 year age range of 22 patients (Fakhrunnisa, 2016). Similar to Supadmi’s (2011) study, patients with the hypertensive disease who underwent hemodialysis had the greatest number in the 46-75 year age range of 42 patients (70.0%) of 60 cases (Supadmi, 2011).

This is in accordance with patients with chronic renal failure who undergo hemodialysis in Indonesia. According to the Indonesian Renal Registry (IRR) in 2011 was accounted for 27% of patients with chronic renal failure who underwent hemodialysis with age range of 45-54 years (IRR, 2011). In this situation similar to Qalbina’s study (2014), there were 30 patients with the chronic renal disease with hemodialysis (50.86%) of the 59 cases with the greatest number in the 50-59 years age range (Qalbina, 2014).

Chronic renal failure is more prevalent in young adulthood. This is because of unhealthy lifestyles such as consuming fast food, stressful
busyness, sitting all day in the office, often drinking coffee, energy drinks, rarely consume water. Bad habits are a risk factor for damage to the kidneys (Dharma, 2015). Pomegranate Research, et al (2017) showed that drinking water $<1000 \text{ml/day}$ increased the risk of chronic renal failure by 7.69 times compared with those who drank $\geq 2000 \text{ml/day}$. Drinking enough water will reduce the occurrence of kidney stone disease that may increase the risk of chronic renal failure (Delima, et al., 2017).

Someone who often consumes energy drinks or the supplement drink has risk of chronic renal disease. In the Latifah study (2016) it states that a person consuming energy drinks $>5 \text{years}$ have a 14-fold risk of suffering from chronic renal failure. Similarly, a person who consumes a 1-5-year-old energy drink has a risk of 7.333 times suffering from chronic renal failure. Energy drinks contain harmful chemicals such as preservatives, dyes, flavours and artificial sweeteners. When consumed continuously then the existing glomerulus kidney undergoes cell, cell destruction or the occurrence of necrosis. The more often the kidney gets damaged faster (Latifah, 2017). However, if consuming energy drinks is not done continuously or not for long periods of time, then it is not a risk factor for the incidence of chronic renal failure (Pranandari, 2015).

Based on the age range of patients, in this study it can be concluded that outpatients with chronic renal failure with hypertension who undergo hemodialysis and get antihypertensive therapy at RSUP dr. Soeradji Tirtonegoro Klaten in the year 2017 obtained the greatest results in the 41-75 years old range of 42 patients with 76% percentage.

4.3. Use of Antihypertensive Drugs and Supporting Drugs

It can be seen in Table 4.3 that it describes the use of drugs based on the name of the drug, drug classes, and the number of patients who get the drug. In RSUP dr. Soeradji Tirtonegoro Klaten 2017 in outpatients with chronic renal failure with hemodialysis in addition to receiving
antihypertensive drugs they also received supportive medications such as anti-gastritis, analgesic-antipyretic, antianginal, antianemia, supplements, vitamins, antifibrinolytics, antidiabetic, anti-gout, and antibiotics.

Table 4.3 Distribution of supporting drug use in outpatients chronic renal failure with hemodialysis at RSUP dr. Soeradj Tirtonegoro Klaten 2017

<table>
<thead>
<tr>
<th>No</th>
<th>Class Therapy</th>
<th>Medicine</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Antihypertensive</td>
<td>Hydrochlorothiazid</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Furosemide</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Irbesartan</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Valsartan</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candesartan</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amlodipine</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Diltiazem (CD</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Nifedipine (Adalat</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bisoprolol</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atenolol</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clonidin</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Anti-gastritis</td>
<td>Lansoprazol</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ranitidine</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Analgesic-Antipyretics</td>
<td>Paracetamol</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>Antiangina</td>
<td>ISDN</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>Supplement</td>
<td>CaCO₃</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>Antianemia</td>
<td>Folic Acid</td>
<td>42</td>
</tr>
<tr>
<td>7</td>
<td>Vitamin</td>
<td>Vit B₁₂</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mecobalamin</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>Antifibrinolytics</td>
<td>Tranexamic Acid</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>Antidiabetic</td>
<td>Glimepiride</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gliquidone</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucodex</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Novorapid</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>Anti-Gout</td>
<td>Allopurinol</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>Antibiotics</td>
<td>Cefixim</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clindamycin</td>
<td>2</td>
</tr>
</tbody>
</table>

(Source: Data of research result)
Seen from Table 4.3, drugs are often prescribed in patients with chronic renal failure with hypertension undergoing hemodialysis of antihypertensive drugs and antianemia drugs. The most commonly prescribed antihypertensive drugs are furosemide and amlodipine. This is similar to the research of Rahim (2017) of antihypertensive drugs in patients with frequent renal failure which are furosemide and amlodipine (Rahim, 2017). Furosemide is the first drug of choice in patients with chronic renal failure with GFR <30ml/minute/1.73m2 or in patients with chronic renal failure with stages 4 and 5. In chronic renal failure patients, furosemide is a drug used as a diuretic (Sari, 2016). While amlodipine is a drug from the class of Calcium Channel Blocker (CCB) which can lower blood pressure is one of the first class of antihypertensive drugs. This CCB class drug has been shown to be very effective in hypertensive patients (Gunawan, 2012).

In this study, patients who obtained furosemide and amlodipine were 43 patients. The most widely used drug use was folic acid. The patients who received folic acid were 42 patients. This situation is similar to the 2013 study of Salwa in hypertensive patients with complications of renal failure in which the most widely used drug is furosemide of 43 patients and folic acid as much as 42 patients (Salwa, 2013). This is similar to the 2016 Winalda study of the most commonly prescribed supportive drugs, folic acid and CaCO$_3$ (Winalda, 2016).

CaCO$_3$ is a calcium supplement drug. According to Tomasello (2008), the inhibition of phosphate excretion in chronic renal failure leads to hyperphosphatemia which physically and chemically leads to hypocalcemia. Thus, in case of hyperphosphatemia and hypocalcemia, it may increase parathyroid hormone. With this, it is necessary to administer phosphate binder agents to prevent the occurrence of hyperphosphatemia. The most commonly used phosphate binder agent is calcium carbonate (Tomasello, 2008).
Folic acid is a drug used as an antianemia. In the study of Hidayat R, et al., (2016) of 67 patients there were 66 patients (98.5%) suffering from anaemia in chronic renal patients and 1 patient (1.5%) did not suffer from anaemia in chronic kidney disease. Folic acid is a water-soluble vitamin and functions in producing red blood cells and prevents the occurrence of anaemia. Folic acid is widely prescribed in patients with chronic renal failure because there is an association between anaemia and chronic renal failure. In which there is the occurrence of an abnormal response of the body in stimulating fibular in producing erythropoietin (EPO). The occurrence of erythropoietin deficiency produced by peritubular cells that can cause anaemia (Hidayat R, et al., 2016). Erythropoietin is a hormone that stimulates the formation of red blood cells or erythrocytes. The occurrence of erythropoietin deficiency results in decreased blood cell formation, such a condition is called anaemia.

4.4. Evaluation of Patient Accuracy

The administration of the drug according to the patient’s condition or the patient’s disease history is called the right patient. It is said exactly the patient if not the occurrence of contraindications to the condition of the patient as well as the accompanying illness.

<table>
<thead>
<tr>
<th>Patient Accuracy</th>
<th>Amount</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Accuracy</td>
<td>55</td>
<td>100%</td>
</tr>
<tr>
<td>Patient Inaccuracy</td>
<td>-</td>
<td>0%</td>
</tr>
</tbody>
</table>

(Source: Data of research result)

Based on Table 4.4 when seen based on patient accuracy in the use of antihypertensive drugs in outpatients with chronic renal failure with hemodialysis in 2017 in RSUP dr. Soeradji Tirtonegoro Klaten it produces
100% precise patient achievement. That is, the drug that has been given to the patient is in accordance with the pathology and physiology of the patient so as not to cause contraindication to the patient.

Irbesartan drugs, valsartan, and candesartan are the drugs of a class of Angiotensin Receptor Blocker (ARB) therapy class. Irbesartan is a cure for hypertension since it can lower blood pressure and can also be used for patients with type 2 diabetes who have high blood pressure. Irbesartan contraindications are hypotension, hyperkalemia, pregnant women, lactating women, and also bilateral renal artery stenosis or stenosis in the only functioning kidney (Gunawan, 2012). Valsartan is a useful drug also for treating hypertension or high blood pressure, heart failure when ACE-I cannot be used, or in conjunction with ACE-I if β-blocker cannot be used. This class of drugs is contraindicated in patients with bile cirrhosis, cholestasis, pregnant women, and also breastfeeding women (Jordan B, et al., 2014-2015). Candesartan medicine is a drug to treat hypertension and also to treat heart problems (Jordan B, et al., 2014-2015). Contraindications to this drug are hypersensitivity to candesartan; severe liver damage and or cholestasis; pregnancy; and breastfeeding (Lacy C, et al., 2008-2009).

Furosemide is a drug class of Loop Diuretics which is a drug for people with oedema caused by heart disease, kidney, and lung. Furosemide is contraindicated in patients with hypokalemia, hyponatremia, anuria, coma (Jordan B, et al., 2014-2015). Hydrochlorothiazide or HCT is a thiazide diuretic class medication that overcomes hypertension. Thiazide is the main drug in the treatment of hypertension used as a single drug or a combination with another antihypertensive (Gunawan, 2012). This thiazide is contraindicated with patients suffering from hypersensitivity to hydrochlorothiazide, thiazides, or other sulphonamide derivatives; anuria; renal decompensation or severe renal impairment (creatinine clearance <30 mL/minute); pregnant women (Lacy C, et al., 2008-2009).
Amlodipine is a remedy for hypertension or high blood pressure and can also be used to treat angina pectoris attacks or sitting wind. It is contraindicated in patients with cardiogenic shock, unstable angina, and significant aortic stenosis (Jordan B, et al., 2014-2015). Diltiazem is a CCB-type drug that serves to treat hypertension and also treat angina. These class drugs are contraindicated with severe bradycardia, left ventricular failure with pulmonary congestion, two- or three-degree AV blockade (except when using a pacemaker), and sinus disease syndrome (Jordan B, et al., 2014-2015). This drug is hypersensitive to diltiazem, serious hypotension (<90 mmHg) (Lacy C, et al., 2008-2009).

Clonidine and nifedipine are Calcium Chanel Blocker (CCB). Clonidine is a drug for treating high blood pressure or hypertension, migraine and also for treating the sensation of heat that is felt when menopause (menopausal flushing) (Jordan B, et al., 2014-2015). The contraindications of this drug are hypersensitivity to clonidine hydrochloride (Lacy C, et al., 2008-2009). Nifedipine is a CCB-type drug that serves to treat angina prophylaxis and also hypertension or high blood pressure. It is contraindicated with cardiogenic shock, advanced aortic stenosis, unstable or acute angina attacks (Jordan B, et al., 2014-2015).

Bisoprolol is a class of β-blocker drugs that can overcome hypertension, angina, and chronic heart failure. It is contraindicated with asthma, uncontrolled heart failure, bradycardia, hypotension, sinus syndrome, two- or three-degree AV block, cardiogenic shock; phaeochromocytoma (Jordan B, et al., 2014-2015). From the description of the above drugs, the absence of contraindications to the condition of the patient or patients with CRF with hemodialysis has been treated with antihypertensive drugs in accordance with the selection of drugs so that no contraindications occur.
4.5. Evaluation of Drug Accuracy

Selection of drugs in accordance with the drug of choice is the most needed when giving medicine to patients. Selection of the right drug will give the right effect, safe, no contraindications with the diseases that accompany and is adjusted to the patient’s blood pressure. This research analyze the exact medicine used the American Society of Hypertension standard.

American Society of Hypertension (ASH) states that in the first stage hypertension with blood pressure of 140/90 mmHg - 159/99 mmHg at <60 years of age using ACE-I or ARB class drug therapy, it can be added with CCB or thiazides, if necessary group CCB + thiazide + ACE-I (or ARB); while at ≥60 years of age use either CCB or thiazide drug therapy, and may be added with ACE-I or ARB class medications, if necessary, CCB + thiazide + ACE-I (or ARB) group. In stage II hypertension with blood pressure ≥160 / 100 mmHg, therapy begins with the use of two drugs or a combination. Namely CCB or thiazide group drugs combined with ACE-I or ARB classes; and if necessary group CCB + thiazide + ACE-I (or ARB) (Weber MA, et al., 2013).

It can be seen in Table 4.5 that this study found the drug inaccuracy as much as 5 cases with a percentage of 9.08%. There were 2 cases (3.63%) of unacceptable drug combinations and irrational therapy of 3 cases (5.45%). According to Sumawa PMR, et al., In his study “Rationale Evaluation of Antihypertensive Drug Usage in Inpatient Hypertension Patients at Prof. DR. R. D. Kandou Manado Period from January to June 2014 “states that the use of incorrect combinations when obtaining two types of drugs of the same class are used simultaneously or are not according to standard (Sumawa PMR, 2015).
Table 4.5  The accuracy of drugs in the use of antihypertensive drugs in outpatients chronic renal failure with hemodialysis at RSUP dr. Soeradji Tirtongegoro Klaten 2017.

<table>
<thead>
<tr>
<th>Category</th>
<th>Antihypertensive Drugs</th>
<th>No. Cases</th>
<th>Explanation</th>
<th>Amount</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect combination of drugs</td>
<td>Irbesartan dan Candesartan</td>
<td>P11</td>
<td>Irbesartan and Candesartan from ARB class</td>
<td>2</td>
<td>3,63%</td>
</tr>
<tr>
<td></td>
<td>Bisoprolol dan Atenolol</td>
<td>P44</td>
<td>Bisoprolol and Atenolol from β-blocker class</td>
<td>3</td>
<td>5,45%</td>
</tr>
<tr>
<td>Irrational therapy</td>
<td>Furosemid, Candesartan, Amlodipin, dan Clonidin</td>
<td>P25</td>
<td>Getting therapy with 4 antihypertensive combinations</td>
<td>3</td>
<td>5,45%</td>
</tr>
<tr>
<td></td>
<td>Furosemid, Candesartan, Amlodipin, dan Clonidin</td>
<td>P49</td>
<td>Getting therapy with 4 antihypertensive combinations</td>
<td>3</td>
<td>5,45%</td>
</tr>
<tr>
<td></td>
<td>Furosemid, Irbesartan, Bisoprolol, Atenolol, dan Diltiazem</td>
<td>P44</td>
<td>Getting therapy with 5 antihypertensive combinations</td>
<td>3</td>
<td>5,45%</td>
</tr>
</tbody>
</table>

(Source: Data of research result)

In case of number P11, the patient was given irbesartan and candesartan drugs. Irbesartan and candesartan drugs are antihypertensive drugs of ARB group. While in the case number P44, the patient received drug therapy bisoprolol and atenolol which is a drug of β-blocker class. The situation is similar to Anita Salwa’s research (2013) where there are 2 cases of patients who get inappropriate drug combination therapy. The first case got the drug diltiazem and amlodipine which is a drug of the CCB class. While in the second case, patients get the drug captopril and lisinopril.
which are drugs of the ACE-I class. Giving two types of drugs of the same class used simultaneously is the use of an unacceptable combination of drugs (Sumawa PMR, 2015), whereas incorrect combination of drug administration can increase undesirable effects so that therapeutic effects are not achieved (Salwa, 2013).

Antihypertensive monotherapy in lowering blood pressure effectively reaches only about 50% of patients. Antihypertensive therapy of two or more different classes is often necessary for adequate blood pressure control (Skolnik, et al., 2000). However, excessive administration of the drug may pose a risk for greater unwanted effects as can the occurrence of interactions, side effects, and intoxication (Ministry of Health RI, 2013).

In this study, we found 5.45% cases in the combination with antihypertensive drugs were as 4 to 5 combinations of drugs. The problem of P25 and P49 get the treatment with 4 antihypertensive combinations of furosemide, candesartan, amlodipine and clonidine. While in case number P44 get therapy with 5 antihypertensive combinations of furosemide, irbesartan, bisoprolol, atenolol, and diltiazem. This is similar to that of Salwa (2013) getting an irrational combination therapy case. There were 6 patients (12%) who received 4 to 5 combination antihypertensive treatments. Many clinical trials suggest that a combination of antihypertensive drugs requires only 2 to 3 combinations to achieve blood pressure targets (Salwa, 2013).

Using a combination of therapy dosage is to get an increase in blood pressure control by using two agents that have a workplace and from different classes. Using low doses of two different ones can also minimize the clinical and metabolic effects that occur with maximal doses of combination tablets. Some researchers recommend using a combination of antihypertensive therapy as an initial treatment especially in patients with target organ damage or more severe initial hypertension (Skolnik, et al., 2000).
4.6. Evaluation of Dosage Accuracy

This study obtained the exact dose results presented in Table 4.6 that were adjusted with Drug Dosing Renal Failure, British National Formulary 68, and Drug Information Handbook 17th. Obtained it can be many as 54 patients (98.19%) doses and inappropriate dosage as much as 1 case (1.81%). Giving the dosage of the drug to the right patient is very important because it can lead to overdose if excessive dosage and effectiveness of the drug in the body decrease if dosage are less.

Table 4.6  The accuracy of dosage in the use of antihypertensive drugs in outpatients chronic renal failure with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017

<table>
<thead>
<tr>
<th>Category</th>
<th>No. Cases</th>
<th>Treatment given</th>
<th>The treatment should be</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive dosage</td>
<td>P44</td>
<td>Atenolol 2 x 50 mg</td>
<td>CrCl 10-30 ml/min, dose used 25-50 mg every day</td>
<td>1.81%</td>
</tr>
</tbody>
</table>

(Source: Data of research result)

The accuracy of the dosage is appropriate in the dosage of the drug. In this study, assessing whether or not a dose of a drug can be analyzed using a reference book Drug Dosing Renal Failure, Drug Information Handbook, and the British National Formulary. The researchers found 1 case of inaccuracy in drug dosing. In the case of P44, it is said that the dosage is not appropriate because of excessive dosing of atenolol. In patients with renal failure with hypertension undergoing hemodialysis, and having a CrCl value of 10-30 ml/min should receive atenolol therapy with a range of 25-50 mg doses per day. However, in this case, patients get atenolol therapy a day 100 mg with two drinks each day.

Giving a dose is very influential in the effects of drug therapy. Excessive dosage, especially for drugs with a narrow range of therapy
will give very risky side effects. Neither with the dose is too low, then the desired therapeutic levels will not be achieved (Kemenkes, 2011). In outpatient patients with chronic renal failure with hemodialysis in RSUP dr. Soeradji Tirtonegoro Klaten 2017 antihypertensive drugs used are ARB, CCB, diuretic, β-blocker, and α-blocker drugs. ARB drugs used include irbesartan, valsartan, and candesartan. Irbesartan in a day required 300 mg once (in hemodialysis or age over 75 years). In the renal disease with type 2 diabetes hypertension, initially they are given 150 mg once daily but it can be increased by 300 mg once daily if it includes hemodialysis or over 75 years of age. And for children is not recommended (Jordan B, et al., 2014-2015). Judging from the book entired Drug Dosing in Renal Failure in a day irbesartan drugs are given with a dose range of 150-300 mg (DeBellis RJ, et al, 2000).

In hypertensive patients they typically get valsartan therapy 80 mg once daily (initially 40 mg once daily in intravascular volume depletion), and can be increased to 320 mg daily. For patients with myocardial infarction, an initial dose of 20 mg is given twice daily and can be increased to 160 mg twice daily if tolerated (Jordan B, et al., 2014-2015). While candesartan drug in a day the maximum dose is 8.32 mg. However, patients with kidney disease dosage should be given starting from low doses (DeBellis RJ, et al., 2000).

Calcium Channel Blocker antihypertensive drugs are used in outpatients with chronic renal failure with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten in 2017 such as amlodipine, diltiazem and nifedipine (Adalat). In the normal dose of the Drug Dosing Renal Failure reference book the dosage for amlodipine 2.5 to 10 mg daily. Diltiazem drug for hypertension is usually 180-240 mg daily and nifedipine 10 mg three times daily or 30 mg once daily (Lacy C, et al., 2008-2009).
Hydrochlorothiazide is a drug belonging to the thiazide diuretic class. Hydrochlorothiazide is used as an antihypertensive drug that aids the kidneys in excreting sodium or liquids that can cause fluid retention. In a day the dose used for hypertensive patients 25-50 mg and for oedema patients can be given doses 25-200 mg/day and the dosage can be divided 1-3 in a day. However, hydrochlorothiazide should not be given to patients with SCr> 2.5 mg/dl (DeBellis RJ, et al., 2000).

4.7. Research Validity

There are some limitations in this research:

1. Many medical records are incomplete and hard to read.
2. Limitations of socio-demographic data of patients.
3. This study only determines the accuracy of drug therapy in terms of patient accuracy, drug accuracy, and accuracy of dosage.
CHAPTER 5
CLOSING

5.1. Conclusion
1. The accuracy of patients in the use of antihypertensive drug therapy in chronic renal failure outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017 obtained 100%.
2. The accuracy of drugs in the use of antihypertensive drug therapy in chronic renal failure outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017 obtained results 90.92% and there is drug inappropriateness of 9.08%.
3. The accuracy of dosage in the use of antihypertensive drug therapy in chronic renal failure outpatients with hemodialysis at RSUP dr. Soeradji Tirtonegoro Klaten 2017 obtained results 98.19% and there is an inaccurate dose of 1.81%.

5.2. Sugestion
1. Further research on the evaluation of drug use should be observed from all drug rationale criteria and using the most recent reference standards.
2. Need for research by looking at patient condition directly so that we can know and follow its development.


Gunawan S.G. 2012. *Farmakologi dan Terapi edisi 5*. Jakarta: Departemen Farmakologi dan Terapeutik FKUI.


LIST OF APPENDICES

Appendix 1 Research Scheme

Research Proposal → Supervisor

Request a research permit to the Head of Pharmacy Department → RSUP dr. Soeradji Tirtonegoro Klaten

Management of research administration → Data collection at Medical Record Interpretation → Processing and analysis of data → Preparation of research results report

Licensing: filed a letter from the Head of Pharmacy Department to the Director of the Hospital → Issue a research permission letter
Appendix 2 Application Permit Letter

PROGRAM STUDI FARMASI
FAKULTAS ILMU KESEHATAN
UNIVERSITAS DARUSSALAM GONTOR

Nomor: 118/UNIDA/FIK-Farmasi-07/1459
Perihal: Permohonan Izin Melakukan Pencetakan

Kepada Yth:
Direktur RSUP dr. Soeradjji Tirtonegoro Klaten

Dengan hormat,

Dalam rangka mendukung program pendidikan dan kegiatan penelitian di Universitas Darussalam Gontor bahwa setiap mahasiswa dalam menyelesaikan studinya diwajibkan melakukan penelitian untuk skripsi yang harus dipenuhi sebagai salah satu syarat dalam menyelesaikan studinya.

Sehubungan dengan hal tersebut kami mohon kiranya dapat diperkenankan untuk melakukan penelitian di RSUP dr. Soeradjji Tirtonegoro Klaten. Adapun mahasiswa yang akan melaksanakan penelitian sebagai berikut:

Nama: Farah Afiqah
NIM: 35.2014.7.1.0956
Program Studi: Farmasi
Fakultas: Ilmu Kesehatan
Judul Pencetakan: Evaluasi penggunaan obat antibakteri pada pasien gajal
Waktu: Oktober 2017 - Januari 2018

Demikian disampaikan atas perhatian dan kerja samanya kami ucapkan terima kasih.

Gontor Putri I, 07 November 2017
Kepala Program Studi Farmasi FIK
Universitas Darussalam Gontor

Surya Amet S.Si. M.Kes. Apt
NIl.Y. 048/2
Appendix 3 A Letter from the hospital

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA
DIREKTORAT JENDERAL PELAYAN KESEHATAN
RSUP dr. SOERADJI TIRTONEGORO
Jln. KIT, dr. Soeradj Tirtonegoro No. 1 Klaten
Telp : (0271) 352 0900 Fax : (0271) 352 0104 E-Mail : rsusoe@sigsoft.com

No. : DP.02.01/1.2.2/21/10/2017

Yth.
Ketua Program Studi Farmasi
FIK Universitas Darussalam Gontor di Ngawi

Menindaklanjuti surat Saudara Nomor 119/UNIDA/PIK-Farm-001/439 tanggal 07 November 2017, Hal permohonan Ijin Pelatihan bersama ini disampaikan bahwa kami tidak beralasan memberikan Ijin kepada mahasiswa Universitas Darussalam Gontor, atas:

Nama : Farah Affiah
NIM : 38261471.0.0566

Untuk menegakkan Ijin Pelatihan guna menyusun Skripsi dengan judul “Evaluasi Penggunaan Obat Antihipertensi pada Pasien Gagal Ginjal Kronik dengan Hemodialisa di Ranat Inap RSUP dr. Soeradj Tirtonegoro Klaten tahun 2017”

Ijin ini berlaku selama liga bulan terhitung diterbitkannya surat hingga liga bulan berikutnya (Pertanggal 30 November 2017 s/d 28 Februari 2018) sesuai dengan ketentuan yang berlaku, apabila dalam batas waktu yang ditentukan tidak selesai maka proses ini harus diperpanjang.

Selanjutnya kepada yang bersangkutan diwajibkan:
1. Merubah peraturan dan bata letih yang berlaku di RSUP Dr. Soeradj Tirtonegoro Klaten.
2. Tidak diterima maklumat penelitian atas pertanyaan data yang tidak sesuai dengan judul penelitian dinilai terlalu.
4. Mempresentasikan hasil penelitiannya di RSUP dr. Soeradj Tirtonegoro

Demikian, atas perhatian dan ke jamais yang baik kami ucapkan terima kasih.

a.n. Direktur Cinta
Direktur Umum SOM dan Pendidikan

drg. Rahmiadyan Mansur, M.Kes
NIP. 195608131987031004
Appendix 4 Data Collection

A. Identitas Pasien

Nama Pasien : 
Nomor Rekam Medik : 
Umur Pasien :  Tahun
Berat Badan :  Kg
Hemodialisa : Tanggal  Bulan  Tahun
Pemberian Obat : Tanggal  Bulan  Tahun
Status Pengobatan : Rawat Jalan

B. Data Laboratorium

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<th>Tgl. Pengukuran</th>
<th>Kadar Normal</th>
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<tr>
<td>1</td>
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<td>0,5-0,9 mg/dl</td>
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<tr>
<td>2</td>
<td>Kadar Cr</td>
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<td></td>
<td>0,5-0,9 mg/dl</td>
</tr>
<tr>
<td>3</td>
<td>Kadar BUN</td>
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<td>8-20 mg/dl</td>
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C. Terapi Obat Antihipertensi

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<tr>
<th>No</th>
<th>Kelas Terapi</th>
<th>Gol</th>
<th>Nama Generic</th>
<th>Dosis Awal (mg/hari)</th>
<th>Dosis Maksimal (mg/hari)</th>
<th>Frekuensi Pemberian</th>
<th>Sediaan</th>
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<tbody>
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</tbody>
</table>
### D. Obat Penunjang

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<th>Dosis Awal (mg/hari)</th>
<th>Dosis Maksimal (mg/hari)</th>
<th>Frekuensi Pemberian</th>
<th>Sediaan</th>
</tr>
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<tbody>
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### E. Diagnosa Pasien

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### F. Riwayat Penyakit

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<td></td>
</tr>
</tbody>
</table>

### G. Keluhan Pasien

<table>
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<td></td>
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Appendix 5 Research control card

<table>
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<th>Kegiatan</th>
<th>TTD</th>
</tr>
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<td>11 Oktober 17</td>
<td>Menerima inis penelitian dari Pak. Soeharto</td>
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<tr>
<td>2</td>
<td>26 Oktober 17</td>
<td>Dapatkan surat tanda dari penda DAUAN ACC penelitian</td>
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<td>3</td>
<td>1 November 17</td>
<td>Pengambilan surat ke RS, u/ mendapatkan administrasi</td>
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<td>4</td>
<td>2 November 17</td>
<td>Pengajuan surat revisi</td>
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<td>5</td>
<td>20 Nov 17</td>
<td>Dapat surat revisi terkait penelitian</td>
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<tr>
<td>6</td>
<td>26 Nov 17</td>
<td>Pengambilan dkti RM</td>
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<td>7</td>
<td>05 Nov 17</td>
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<td>8</td>
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<td>KEGIATAN</td>
<td>TTD</td>
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<td>13</td>
<td>17 Nov 2017</td>
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<td>06 Des 2017</td>
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</table>

Mantingan, 3 Januari 2018
Dosen Pembimbing.

Surya Asad, S.Si., M.Kes., Apt
NIDN: 1716096901
Appendix 6 Documentation
Appendix 7 Patient data
<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Duration</th>
<th>Activity</th>
<th>Heart Rate (bpm)</th>
<th>Elevation Gain (ft)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/9/2017</td>
<td>9:00</td>
<td>1:30</td>
<td>Running</td>
<td>180</td>
<td>50</td>
</tr>
<tr>
<td>12/9/2017</td>
<td>9:30</td>
<td>1:15</td>
<td>Cycling</td>
<td>140</td>
<td>20</td>
</tr>
<tr>
<td>12/9/2017</td>
<td>11:15</td>
<td>1:00</td>
<td>Hiking</td>
<td>120</td>
<td>10</td>
</tr>
<tr>
<td>12/9/2017</td>
<td>12:15</td>
<td>1:10</td>
<td>Swimming</td>
<td>160</td>
<td>30</td>
</tr>
<tr>
<td>12/9/2017</td>
<td>1:25</td>
<td>1:30</td>
<td>Yoga</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>12/9/2017</td>
<td>2:55</td>
<td>1:45</td>
<td>Walking</td>
<td>110</td>
<td>15</td>
</tr>
</tbody>
</table>

**Notes:**
- Heart rate data was collected using a heart rate monitor.
- Elevation gain data was recorded using a GPS device.
- Activities were completed at an outdoor setting.

**Equipment Used:**
- Heart Rate Monitor
- GPS Device
- Swimming Goggles
- Yoga Mats
- Walking Shoes
- Cycling Bike