EFFECT OF PATIENTS TAKING AMLODIPINE ON UREA LEVELS

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ABSTRACT

Background: Hypertension is a condition when blood pressure increases or is often referred to as a "silent killer" because signs and sympotoms occur, usually causing headaches, nosebleeds, irreguler heartbead, fan buzzing in the ears, hypertension is a disease that is often found among elderly. Research Purposes: To determine the effect of patients taking amlodipine on urea levels. Research Methodos: Analytic observational research with cross sectional research design. Used 24 sampels of hypertension who consumend the drug amlodipine and analyzed the data using a non parametric test. Result: The mean results of examining urea levels in patients taking amlodipine were 31,61. Conclusion: There wa a significant effect of patients taking the drug amlodipine on urea levels according to adherence in taking the a p value of 0,003 (p<0,05). The results of blood pressure meansurements of patients taking the drug averaged 145 mg/dl.

| KEYWORDS | *Amlodipine Drugs, Urea Level* |

INTRODUCTION

Hypertension is an increase in arterial blood pressure with a systolic pressure of more than 140 mmHg and a diastolic pressure of more than 90 mmHg. Hypertension is often referred to as a silent killer, because it is a deadly disease, without realizing the symptoms first. (Hero et al., 2013).

Generally, hypertension has no specific cause. Hypertension occurs in response to increased cardiac output or increased peripheral pressure. However, there are several factors that influence the occurrence of hypertension, among others: genetics, obesity, smoking, gender, stress, lack of exercise. (Nuraini, 2015).

According to data from the World Health Organization (WHO) in 2018 shows that around 1.13 billion people in the world have hypertension, meaning that 1 to 3

people in the world are diagnosed with hypertension. The number of people with hypertension continues to increase every year, it is estimated that by 2025 there will be 1.5 billion people affected by hypertension, and it is estimated that every year 10.44 million people die from hypertension and its complications. The prevalence of hypertension based on the results of measurements in the population in Indonesia at the age of 18 years is 34.1%, the highest in South Kalimantan (44.1%), while the lowest in Papua is (22.2%). Hypertension occurs in the age group 31-44 years (31.6%), age 45-54 years (45.3%), age 55-64 years (55.2%). The prevalence of hypertension in Indonesia is 31.7% which means that almost 1 in 3 people aged 18 years and above suffer from hypertension. There are various factors related to genetics and lifestyles such as lack of physical activity, smoking and drinking alcohol that play a role in the high rate of hypertension. (Hidayat & Agnesia, 2021).

The length of consumption of amlodipine drugs for 6-7 years and in the period of treatment, where amlodipine drugs are standard drugs given to people suffering from hypertension. The most specific side effect in patients taking amlodipine is edema, but there are also several side effects that can be found in the use of amlodipine such as nausea, vomiting, abdominal pain, dry mouth, constipation, gingival hypertrophy, dizziness, headache and insomnia, palpitations, chest pain abnormalities, photosensitivity reactions, frequent urination (polyuria) and an increase in enzymes in the liver. (Tiyas, 2021).

Amlodipine works by inhibiting calcium ions from entering the vascularization of smooth muscle and heart muscle so as to reduce blood pressure. (Alawiyah & Mutakin, 2017). If you continue to take the drug in the long term, it can damage the kidneys. One of the other functions of the kidneys is to excrete the end products or metabolic waste of the body, such as urea, uric acid, and creatinine. If these metabolic waste products are allowed to accumulate, they can become toxic to the body, especially the kidneys, which will cause problems if the kidneys fail. The results of body metabolism such as ureum will increase, if kidney function is only 5% or less. (Arjani, 2017).

The effect of elevated blood urea levels depends on the degree of LFG impairment. At an LFG of 60%, the patient has not felt any complaints but there has been an increase in serum urea and creatinine levels. At 30% LFG, complaints such as nocturia, weakness, nausea, poor appetite, and weight loss begin to occur. At LFG <30%, patients show symptoms and signs of uremia, such as anemia, increased blood pressure, nausea and so on, (Irendem K.A. et al., 2016)

The difference with previous studies chose ureum because, ureum is one of the parameters for examining kidney function which is more specific than uric acid. The drug amlodipine is also consumed for 12 years with other diseases such as: gout, cholesterol.

This study aims to determine whether consumption of amlodipine affects blood urea levels in hypertensive patients. The specific objectives of this study are to measure blood pressure and examine ureum levels of patients taking amlodipine and analyze the effect. The hypothesis of this study is that there is an effect of hypertension drug consumption on blood urea levels. The benefit of this study for the researcher is to increase knowledge and insight into the topic, while for the

institution is to provide information about the effect of hypertension drug consumption on blood urea levels.

Literature Review
Hypertension
Definition of Hypertension

Hypertension is one of the non-communicable diseases with a high prevalence rate in the world. WHO (World Health Organization) in 2015 estimated a worldwide incidence rate of around 972 million people or 26.4% of people worldwide have hypertension, this figure is likely to increase to 29.2% in 2025, an increase in systolic blood pressure greater than 140 mmHg and or diastolic greater than 90 mmHg on two measurements with an interval of 5 minutes in a state of adequate rest. Hypertension is better known as high blood pressure disease, hypertension is a disturbance in blood vessels that results in the supley of oxygen and nutrients, which are carried by the blood so that it is blocked to the body tissues that need it. (Setia & Nusadewiarti, 2022).

a. Hypertension Factors

Some of the factors that can increase the risk that plays a role in increasing the incidence of hypertension are age, gender, family history, genetics, smoking habits, salt consumption, consumption of saturated fats, use of cooking oil, consumption of alcoholic beverages, obesity, lack of physical activity, stress, lack of knowledge of hypertension, use of estrogen. Hypertension in the elderly is generally accompanied by more severe risk factors, and high or very high cardiovascular risk. Therefore, the management of hypertension in the elderly requires much greater attention. (Setia & Nusadewiarti, 2022).

a) Salt consumption

Salt consumption can cause high blood pressure associated with the occurrence of essential hypertension, as seen from epidemiological studies of the blood pressure of people who consume too much salt. Therefore, since most of them suffer from hypertension, there must be differences in sensitivity to salt. A salt/sodium-sensitive blood pressure response is defined as an average increase in arterial blood pressure of = 5 mmHg after 2 weeks of high salt consumption. Several studies have shown that reducing salt consumption can reduce systolic blood pressure by an average of 3-5 mmHg, with a greater effect in older people with severe hypertension. Howe et al's study on adolescents, however, could not prove a blood pressure lowering effect after reducing dietary salt consumption. In adolescents, sensitivity to salt/sodium occurs in conjunction with other predisposing and risk factors for hypertension, including race, family history of hypertension and obesity, so it is not an independent causative factor for hypertension. (Saing, 2016).

b) Alcohol consumption

There is an association between alcohol consumption and blood pressure status. However, hypertension is a type of disease that has many risk factors, so it is possible that those who do not consume alcohol can also develop hypertension. However, if a person consumes alcohol, then the risk of developing hypertension will also increase, almost 5-20% of cases of hypertension are estimated to occur due to excessive alcohol consumption (Raihan et al., 2014).

c) The association of obesity with the incidence of hypertension.

There is a statistically significant relationship between obesity and the incidence of hypertension. based on the analysis, the OR = 6.47 value is obtained and means that obese people have a risk of developing hypertension 6.47 times compared to people who are not obese. So it can be concluded that obesity is a risk factor for hypertension, there is a relationship between body weight and hypertension, if body weight increases above ideal body weight, the risk of hypertension will also increase. (Nelli et al., 2016).

d) Lack of Physical Activity

Lack of physical activity can also increase the risk of hypertension because it increases the risk of being overweight. Inactive people also tend to have a higher heart rate frequency so that the heart muscle has to work harder with each contraction. The harder and more often the heart muscle has to pump, the greater the pressure on the arteries. (Nelli et al., 2016).

e) Relationship between stress and hypertension

There is a statistically significant relationship between stress and the incidence of hypertension. Based on the analysis, the OR = 0.19 value was obtained and means that people who have a history of stress are at risk of developing hypertension by 0.19 times compared to people who have a history of stress. It can be concluded that stress is a risk factor for hypertension. There is a significant relationship between stress and the incidence of hypertension (Nelli et al., 2016).

f) Genetic Factors

The presence of genetic factors in certain families will cause the family to have a risk of suffering from hypertension. People who have parents with a history of hypertension have twice the risk of suffering from hypertension than people who do not have a family history of hypertension. (Sylvestris, 2017).

g) Age

The age factor also affects the occurrence of obesity. Obesity is also related to age, because as age increases, the metabolism that occurs in the body decreases, which will occur biologically, namely decreasing the function of muscles and increasing fat levels in the body. The older a person is, the movement or activity can cause muscle mass in the body to tend to decrease which can cause a delay in the rate of burning calories in the body. The older a person gets and with a fixed calorie intake, the more difficult it is for the body to burn incoming calories so that there is an accumulation of energy in the body and has an impact on obesity. Actually, among all the controllable risk factors for hypertension, body weight is one of the most closely related to hypertension. Overweight is a hallmark of the hypertensive population. Epidemiological investigations prove that obesity is a hallmark of the hypertensive patient population. It is estimated that as many as 70% of new cases of hypertension are adults who are gaining weight. (Dwi Anggraini et al., 2018)..

h) Gender

There is a significant relationship between gender and blood pressure. Other studies on hypertension also found a significant relationship between gender and blood pressure. Other research on hypertension. The prevalence of hypertension in men is the same as in women. However, women are protected from cardiovascular disease before menopause. Women who have not experienced menopause are

protected by the hormone estrogen which plays a role in increasing HDL levels. High HDL cholesterol levels are a protective factor in preventing atherosclerosis. The protective effect of estrogen is thought to be an explanation of female immunity at premenopausal age. (Raihan et al., 2014).

b. Pathogenesis

The pathophysiology of hypertension is through the formation of angiotensin II from angiotensin I by angiotensin I *converting enzyme* (ACE). ACE plays an important physiological role in regulating blood pressure. Blood contains angiotensinogen which is produced in the liver. This is converted into angiotensin I by the hormone renin. By ACE found in the lungs, angiotensin I is converted into angiotensin I (Putri et al., 2022). (Putri et al., 2022).

The pathogenesis of essential hypertension is still poorly understood. Several studies on blood pressure suggest that there is a relationship between genetics and environment that can influence blood pressure in children and adolescents for the occurrence of essential hypertension. Therefore, the etiology of essential hypertension is complex, including predisposing factors such as race, gender, family history/genetics and influencing factors such as salt consumption, smoking, alcohol consumption, stress and obesity. (Saing, 2016).

c. Etiology

Hypertension is a major cause of morbidity and mortality, accounting for 17 million deaths worldwide each year or 31% of all mortality. In Europe, this figure is as high as 42%. Cardiovascular disease is often associated with lifestyle (smoking, lack of physical activity, unhealthy eating behavior, and genetic stress of excessive salt consumption) and several other risk factors such as hypertension, dyslipidemia, obesity, age, family history of cardiovascular disease, and endothelium dysfunction. (Suling, 2018).

d. Epidemiology

In the world about 970 million people suffer from hypertension, it is estimated that by 2025 there will be about 1.56 billion adults suffering from hypertension. And the American population over 20 years old suffering from hypertension has reached 74.5 million, but almost about 90-95% of cases have no known cause. According to various studies, the overall incidence of hypertension is the same between men and women but differs with age. For those under 45 years old, high blood pressure is more common in men than in women. Then those aged more than or equal to 65 years old are more common in women than men. Blood pressure values increase with age and are very common in older people. African Americans are more likely to develop hypertension at an earlier age (31% in women and 33% in men). In Mexican Americans, hypertension is about 29% in women and 30% in men. Based on the results of blood pressure measurements in Indonesia, the prevalence of hypertension in the population aged 18 years and over in Indonesia in 2013 was 25.8%, with the highest prevalence in Bangka Belitung province (30.9%) and the lowest in Papua (16.8%). (Sulistiawati, 2021).

e. Complications

Complications of hypertension have a considerable impact on health quality of life. Complications that can occur in hypertension based on cohort studies that have been conducted are among others, data from many countries, the reduction in stroke mortality is about 5% per year due to the decreased incidence of cerebrovascular complications associated with primary preventive measures, especially the detection and treatment of hypertension. Other studies report that complications of hypertension can develop during pregnancy, and will increase the risk of hypertension, stroke and coronary heart disease in later life, Other complications that occur in mild hypertension and moderate hypertension affect the eyes, kidneys, heart and brain. In the eyes in the form of retinal hemorrhage, visual impairment up to blindness. Heart failure is a disorder that is often found in severe hypertension in addition to coronary and myocardial abnormalities. In the brain there is often bleeding caused by rupture of microaneurysms which can result in death. (Fitri, 2015).

f. Diagnosis
   1) Anamnesis

In patients with essential hypertension, there are generally no complaints. If complaints arise, they can include headache, anxiety, palpitations, dizziness, stiff neck, blurred vision, chest pain, easy fatigue, and impotence. Headache is common in severe hypertension, with characteristic occipital region pain especially in the morning. Then there is an increase in body weight, lifestyle factors (job changes cause patients to travel and eat outside the home), decreased frequency or intensity of physical activity, or old age in patients with a family history of hypertension.

   2) Physical Examination

In the preparation stage, the patient is relaxed and sits in a chair for >5 minutes. Patients should empty their bladder and avoid caffeine, smoking, and exercise 30 minutes prior to measurement. Neither the patient nor the examiner should talk during preparation and measurement. Blood pressure measurements must be taken with a periodically calibrated device. The patient's arm is placed on the table, the position of the cuff on the patient's arm is at the level of the right atrium (mid-sternum). The size of the cuff must be appropriate. In the first measurement, blood pressure is measured in both arms, the next measurement uses the arm with the highest blood pressure. Repeat the measurement with a pause of 1-2 minutes. Palpation is performed on the radial pulse to determine the systolic when pulsation disappears, then the cuff is developed again by 20-30 mmHg. Decrease the cuff at a rate of 2 mmHg per second, while listening to the korotkoff sound. Use the average of ≥ 2 blood pressure measurements on ≥ 2 occasions to determine blood pressure. (Sulistiawati, 2021).

g. Types of drugs

There are drugs that can be used to lower blood pressure, namely Alpha Blockers (eg: Doxazosin, Prazosin, Alfuzosin Pentolamin), Beta blockers (eg: Propanolol, atenolol, betaxolol, carteolol, nadolol, pindolol), ACE Inhibitors (eg: captopril, lisinopril, moexipril, quinapril, ramipril, trandolapril), Diuretics (eg. hydrochlorothiazide, chlortalidone), calcium channel blockers (eg: Amlodipine,

diltiazem, felodipine, nifedipine, verapamil): Hydrochlorothiazide, chlortalidone), Calcium channel blockers (eg: Amlodipine, diltiazem, felodipine, nifedipine, verapamil), Centrally acting sympathoplegic drugs (clonidine, guanabenz, guanfacine, methyldopa), Vasodilators (eg: Diazoxide, fenoldopam, hydralazine, minoxidil), Angiotension Receptor blockers (eg: Cabdesartan, eprosartan, irbesatran) (Hero et al., 2013).

Amlodipine treatment by inhibiting calcium ions from entering the vascularization of smooth muscle and heart muscle so as to reduce blood pressure. Apart from being an antihypertensive agent, amlodipine can also be used for the treatment of angina pectoris by increasing blood flow to the heart muscle. (Alawiyah & Mutakin, 2017).. The kidney has an important role to maintain the stability of volume, electrolyte composition, and osmolarity of extracellular fluid. Another important function of the kidneys is to excrete end products or metabolic waste, such as urea, uric acid, and creatinine. If these metabolic waste products are allowed to accumulate, they can become toxic to the body, especially the kidneys and cause side effects that disturb most patients. (Arjani, 2017).

h. Classification of Hypertension
Based on the cause of hypertension is divided into 2 groups, namely:
1. Primary hypertension or essential hypertension Primary hypertension or essential hypertension is of unknown cause or also called idiopathic hypertension. Influencing factors such as family history (genetic), environment, hyperactivity of the sympathetic nervous system, renin angiotensin system, increased intracellular Na and Ca and factors that increase risk such as obesity, alcohol, smoking and polycythemia.
2. Secondary hypertension or renal hypertension is hypertension caused by other diseases, the specific causes of which are the use of estrogen, and hormonal disorders, heart disease, diabetes milletus, kidney failure, and vascular or pregnancy-related diseases. (Suling, 2018).

Based on its form, hypertension is divided into 3 namely hypertension, systolic, hypertension, diastolic and mixed hypertension: *Systolic hypertension* (*isolated* systolic hypertension) is an increase in systolic pressure without an increase in diastolic pressure and is commonly found in the elderly. Systolic pressure is related to the high pressure in the arteries when the heart contracts (heart rate). Systolic pressure is the maximum pressure in the arteries and is reflected in blood pressure readings as a greater upper pressure. Diastolic hypertension is an increase in diastolic pressure without an increase in systolic pressure, usually found in children and young adults. Diastolic hypertension occurs when small blood vessels narrow abnormally, thereby increasing the resistance to blood flow through them and increasing their diastolic pressure. Diastolic blood pressure relates to arterial pressure when the heart is in a state of relaxation between two beats. Mixed hypertension is an increase in both systolic and diastolic pressure. (Suling, 2018).

Ureum
a. Definition of ureum

Ureum is the end product of protein and amino acid metabolism produced by the body. High ureum levels are 8 times more common among people with hypertension than other individuals with normal blood pressure. High ureum levels can lead to the additional complication of uremic shock which can lead to death. The level of ureum in the blood is a benchmark that shows the balance between production and excretion by the kidneys. (Malisan et al., 2015).

The plasma concentration of urea is determined by synthesis in the liver and excretion through the urine. Blood urea levels increase with high protein diets, digestive system bleeding, loss of body fluids, impaired renal function, lower urinary tract obstruction and increased protein catabolism. (Rahmawati, 2018). The state of kidney failure characterized by very high plasma ureum levels is recognized as uremia. This condition can be risky and requires hemodilysis or kidney transplantation. (Nuroini & Wijayanto, 2022).

b. Metabolism of ureum

Ureum is the end product of amino acid metabolism. In catabolism proteins are broken down into amino acids and deaminated ammonia. Ammonia in this process is synthesized into urea. Ureum is the waste product of protein breakdown in the body. The urea cycle (also called the ornithine cycle) is the reaction of converting ammonia (NH3) into urea (CO(NH2)2) This chemical reaction occurs mostly in the liver and a little in the kidneys. The liver becomes the center of converting ammonia into urea related to the liver's function as a place to neutralize toxins. Urea is toxic so it is harmful to the body if it continues to accumulate in the body. Increased urea in the blood can be characterized by kidney problems. (Irendem K.A. et al., 2016).

c. Factors affecting ureum levels

The level of ureum in the blood is influenced by many factors, including the following:

1) Severe dehydration

Dehydration is a fluid balance disorder in which the body lacks fluid, but the body excretes more fluid. The kidneys produce urine, which is directly related to fluid in the body. The body wants enough fluid to metabolize, if there is less fluid in the body then the blood and blood pressure will be disturbed. Dehydration can also be affected by kidney performance becoming heavier (Sari & Nindya, 2018).

2) Consumption of drugs

Medications are also a factor in increasing ureum levels in the blood are: Nephrotoxic, Diuretics (Hydrochlorothiazide (Hydrodiuril), Ethacrinic acid (Edecrin. Furosemide (Lasix). Trimteren (Dyrenium), Antibiotics (Basitrasin, Cephaloridin (large doses), Gentamicin, Kanamycin), Chloramphenicol (Choloromycetin), Antihypertension (Methyldopa (Aldomet), Guanetidin (Ismelin), Sulfonamides, Propranolol, Morphine, Lithium carbonate, and Salicylates. (Irawan, 2014).

3) Damage to the kidneys

The damage that occurs in the kidney organ is also caused by decreased kidney function. Decreased kidney function is characterized by increased ureum levels. If only 10% of the kidneys are functioning then the patient is already in the endstage

renal disease (ESRD) stage, which is the final stage of kidney disease. Damaged kidneys will not be able to filter incoming ureum, so ureum levels will enter the bloodstream. This situation is caused by the body failing to maintain metabolism, fluid and electrolyte balance resulting in uremia, which is the retention of urea and other nitrogenous waste in the blood. (Khanmohamadi, 2014).

4) Protein intake in the body

Ureum in the body is the final residue of protein metabolism which is excreted through the kidneys in the form of urine, the more protein intake into the body, the higher the ureum level. Ureaum metabolism is carried out in the kidney organ, if a person's protein intake is too high and is not balanced with other nutritional intake, the kidneys will work hard to break down the protein into amino acids, so that ureum levels in the blood will continue to increase. (Putri et al., 2022).

d. Clinical Overview of Ureum

1) Low Plasma Urea (Uremia)

Decreased ureum levels may be caused by malnutrition or dietary protein intake. Uremia may occur in late pregnancy, due to increased protein synthesis and glomerular filtration. Acute hepatic necrosis causes ureum levels to decrease, as amino acids are not metabolized further into the liver. Low plasma urea also occurs in liver cirrhosis caused by reduced synthesis due to water retention and high rates of protein anabolism, this situation arises during treatment with intensive androgens for example in breast carcinoma and long-term protein malnutrition. (Nuroini & Wijayanto, 2022).

2) High Plasma Urea (Azotemia)

High plasma urea is one of the main abnormal features and its causes are classified as follows:

a) Increased tissue protein catabolism is accompanied by a negative nitrogen balance, such as in fever, atrophic diseases, thyrotoxicosis, diabetic coma or after trauma or major surgery. If the increase in protein catabolism is small, and there is no primary or secondary renal damage, then urinary excretion will remove the excess urea and there is no significant increase in plasma urea.

b) Excessive plasma protein breakdown, such as in patients with leukemia, the release of lekocyte proteins supports high plasma urea.

c) Reduced urea excretion is the main and most important cause and can be prerenal, renal or postrenal. Decreased peripheral blood pressure (as in shock) or venous confinement (as in congestive heart failure) or low plasma volume and hemoconcentration (as in sodium depletion from any cause including Addison's disease), reduce plasma flow to the kidneys. Glomerular filtration for urea is low and there is an increase in plasma urea, in mild cases, if there is no permanent damage to the renal structure, then plasma urea will return to normal when the preenal state is restored to normal.

d) Obstruction of the urine outlet such as an enlarged prostate gland causes high plasma urea.

e) Kidney disease that is accompanied by a decrease in glomerular filtration rate which causes high plasma urea.

e. Ureum Level Check

Examination of serum ureum levels can be used as a test parameter for kidney function, hydration status, assessing nitrogen balance, assessing the progressivity of kidney disease, and assessing hemodialysis results (Verdiansah, 2016). The method used to check serum ureum levels is the enzymatic method. The working principle is that urea is catalyzed into ammonium carbonate by the enzyme urease where the reaction rate depends on the concentration of glutamate dehydrogenase. (Rahmawati, 2018).

Relationship between Hypertension and Ureum Level

Hypertension is a disease of high blood pressure. The blood pressure limit that can be used as a reference to determine whether blood pressure is normal or not is the systolic and diastolic pressure at two measurements 5 minutes apart in a state of complete rest (calm). Hypertension is a disturbance in blood vessels that results in the supply of oxygen and nutrients carried by the blood being obstructed to the body tissues that need it. A person experiences hypertension based on the JNC (*joint national committee*) if the systolic blood pressure (the top) is 140 mmHg or the diastolic blood pressure value A history of hypertension is associated with the incidence of chronic kidney failure. Clinically, a history of hypertension has a 3.2 times greater risk of developing chronic kidney failure. (Suling, 2018).

Hypertension and chronic renal failure affect each other. Hypertension can cause chronic renal failure, while chronic renal failure can cause hypertension. Prolonged hypertension can lead to structural changes in arterioles throughout the body, characterized by fibrosis and hyalinization of blood vessel walls. The main target organs are the heart, brain, kidneys and eyes. Arteriosclerosis in the kidney due to prolonged hypertension causes nephrosclerosis which is the result of ongoing ischemia due to narrowing of the lumen of the intrarenal blood vessels. Blockage of arteries and arterioles will cause glomerular damage and tubular atrophy, so that all nephrons are damaged and cause chronic kidney failure. (Nelli et al., 2016).

Ureum is the end product of protein and amino acid metabolism produced by the liver and distributed through intracellular and extracellular fluids into the blood to be filtered by the glomerulus, The excretion of ureum in the body is approximately 25 mg per day. (Irendem K.A. et al., 2016).. Measurement of blood ureum concentration is done if the kidneys do not excrete enough ureum then blood ureum will continue to increase above normal levels. The normal value of ureum is 20 - 35 mg/dl. Elevated blood ureum or BUN (blood urea nitrogen) levels are an indication of kidney damage. (Suling, 2018).

The kidney is the main organ for removing metabolic waste that is not needed by the body. The main function of the kidneys is to excrete end products or metabolic waste such as ureum, creatinine and uric acid. These metabolic waste, if allowed to accumulate, can be toxic to the body, especially the kidneys. Kidney disease is a disease caused because the kidney organ has decreased function until finally the kidneys are unable to do their job properly. Impaired kidney function

occurs when the body fails to maintain metabolism and fluid and electrolyte balance, causing retention of ureum and other nitrogenous waste in the blood. Impaired kidney function is caused by several factors, one of which is hypertension. The case of hypertension in Indonesia in 2016 was 32.4%. (Irendem K.A. et al., 2016)..

Hypertension and chronic renal failure affect each other. Hypertension can cause chronic renal failure, and chronic renal failure can cause hypertension. Prolonged hypertension can result in structural changes in arterioles throughout the body, characterized by fibrosis and hyalinization of blood vessel walls. The main target organs are the heart, brain, kidneys and eyes. Arteriosclerosis in the kidney due to long-standing hypertension causes nephrosclerosis which is a direct result of ischemia due to narrowing of the lumen of the intrarenal blood vessels. Blockage of arteries and arterioles will cause glomerular damage and tubular atrophy, so that all nephrons are damaged and cause chronic renal failure. (Ningtyas et al., 2019)

RESEARCH METHOD

This study was conducted at the Clinical Chemistry Laboratory of Praya Hospital from January to May 2023 with a cross-sectional analytical observational design, because it is considered easier and more efficient. (Yayan Heryanto, 2010). The study population was hypertensive patients, with a sample of hypertensive patients taking amlodipine. The sample size was calculated using the Lemeshow formula, resulting in 24 samples taken by purposive sampling based on the criteria of length of drug consumption and age. The independent variable was amlodipine, and the dependent variable was blood urea level. Data were collected through laboratory examinations and direct interviews with respondents, and analyzed using the SPSS rank spearman statistical test.

RESULT AND DISCUSSION

Research overview

This study was conducted from January 2023 to May 2023 at Praya Regional Hospital. By using 24 samples suffering from hypertension with the number of female patients as many as 15 people, and men as many as 9 hypertensive patient criteria. The average age of female and male patients is 53.25%, with a blood pressure of 161 mg/dl, and an average ureum level of 31.61, and their compliance with taking the drug is 42% who are obedient, and 58% who are not obedient to taking the drug. For a description of age, gender, blood pressure, can be seen in the description table below:

Table 4.1 Examination results of blood ureum levels of patients taking drugs

Code sample	Gender	Age (TH)	Blood Pressure (mmHg)	Ureaum level (mg/dl)	Description	Duration of drug consumption
1.	Male	51	165	39.7	Compliant	7 Years
2.	Female	41	145	35,2	Compliant	5 Years
3.	Male	54	160	19,7	Non-compliant	7 Years

4.	Female	41	145	30,8	Compliant	6 Years
5.	Female	31	160	35,2	Compliant	7 Years
6.	Female	42	140	60,6	Compliant	7 Years
7.	Female	45	165	36,4	Compliant	6 Years
8.	Female	50	140	19,8	Non-compliant	7 Years
9.	Female	40	160	23,7	Non-compliant	7 Years
10.	Female	60	155	24,3	Compliant	6 Years
11.	Female	55	145	40,5	Compliant	7 Years
12.	Female	50	165	27,9	Non-compliant	7 Years
13.	Female	51	165	32,7	Compliant	7 Years
14.	Male	70	145	24,4	Non-compliant	6 Years
15.	Female	65	164	35,5	Compliant	6 Years
16.	Female	45	165	20,5	Non-compliant	6 Years
17.	Male	55	145	32,5	Non-compliant	7 Years
18.	Female	50	160	23,3	Non-compliant	7 Years
19.	Female	65	145	24,3	Non-compliant	7 Years
20.	Male	70	165	24,9	Non-compliant	6 Years
21.	Male	61	145	42,1	Compliant	6 Years
22.	Male	60	165	35,3	Compliant	7 Years
23.	Male	61	145	33,5	Compliant	7 Years
24.	Male	65	165	33,8	Compliant	6 Years
Average		53,25	161	31,61		

Based on the data from the examination of blood pressure in patients with hypertension, the average examination data obtained has a history of hypertension above normal. With normal ureum values of 10-50 mg/dl.

Data Analysis

The results of the study were processed non-parametrically using the SPSS application. The test in this study used the sperman rank test which aims to determine whether there is an effect of examining patients who take amlodipine drugs on ureum levels, while the results of the sperman rank test can be seen in the table.

Table 4.2 Sperman rank test results using spss on ureum levels

Correlations

			Kepatuhan	Ureum
Spearman's rho	Jenis Kelamin	Correlation Coefficient	-.044	-.056**
		Sig. (2-tailed)	.840	.795
		N	24	24
	Usia	Correlation Coefficient	.251**	.022
		Sig. (2-tailed)	.237	.917
		N	24	24
	Tekanan darah	Correlation Coefficient	-.083	-.050
		Sig. (2-tailed)	.701	.816
		N	24	24
	Kepatuhan	Correlation Coefficient	1.000	-.586
		Sig. (2-tailed)	.	.003
		N	24	24
	Ureum	Correlation Coefficient	-.586	1.000
		Sig. (2-tailed)	.003	.
		N	24	24

Based on the table above, the results of the examination of ureum levels with gender show the probability value (p) is 0.795> 0.05, then Ho is accepted Ha is rejected, which means that there is no influence on the results of ureum on patients who take amlodipine.

Based on the results of the examination of ureum levels according to age, the probability value (p) is 0.917.>0.05 Ho accepted Ha rejected which means there is no influence on ureum levels. While the results of the examination of ureum levels according to blood pressure showed a probability value (p) of 0.816>0.05 Ho accepted Ha rejected which means there is no effect of patients taking amlodipine. Then based on the results of the examination of ureum levels according to drug consumption compliance, the probability value (p) is 0.003 <0.05 Ho accepted Ha rejected, which means that there is an influence of patients taking amlodipine drugs on ureum levels.

Discussion

The results showed that there was an effect of adherence to taking amlodipine drugs in hypertensive patients at the Praya Community Health Center. (Haldi et al., 2020). The result of the probability significance value (p) is 0.003 <0.05 Ho. So that Ha is rejected, which means that there is an effect of patients taking amlodipine on urea levels. Most patients are compliant in using amlodipine drugs. Compliance is influenced by several factors that make the patient's ability to follow optimal care often disrupted by several barriers, including: socioeconomic factors, the health care system, disease characteristics, disease therapy and patient-related factors.(Haldi et al., 2020)

Patients who are not compliant with taking amlodipine drugs are one of the risk factors that can cause an increase in the incidence of morbidity and mortality of patients with hypertension is the patient's non-compliance in taking antihypertensive drugs recommended by the doctor. The quality of life of hypertensive

patients is influenced by adherence to antihypertensive therapy, lifestyle modifica-tions, and the type of pharmacological therapy consumed.(Nurmalita et al., 2019)

Kidney damage can be measured using the examination of creatine and ureum levels in the patient's serum. The normal value of ureum levels is 10-50 mg/dl (Di-arti *et al*., 2019). However, in the research that has been done, patients who take amlodipine have an effect on increasing ureum levels due to non-compliance with taking the drug.

If blood urea levels are too high, kidney damage should be suspected. Acute renal failure is the rapid deterioration of the kidneys' ability to clear the blood of toxic materials, leading to the accumulation of metabolic waste in the blood (e.g. urea). Acute renal failure is a clinical condition characterized by a sudden decrease in kidney function with a consequent increase in metabolites such as urea. (Malisan et al., 2015).

The results showed that the characteristics of most respondents, patients who consumed more drugs in women but after women monopause the risk of developing hypertension between men and women became the same. However, this is not a benchmark that women have higher ureum levels because several other studies, one of which was conducted by Anitia Irawan (2014) showed that ureum levels have no effect on gender. The difference in the number of male and female respondents in this study and other studies can occur due to differences in the number of samples studied.

Based on the age level of the respondents, most experienced hypertension at the age of around 60-65 people as in general the older a person is, it will increase the risk of developing hypertensive disorders. The absence of influence on ureum levels, because what causes ureum levels to increase, lack of fluid in the body (de-hydration) and side effects from the use of drugs in line with previous research (Nurhayati et al., 2021).

One of the causes of increased blood ureum and creatinine levels is uncon-trolled hypertension. Increased blood pressure can cause a decrease in the ability of kidney function to be disrupted, resulting in increased blood urea levels. (Haldi et al., 2020)

Blood pressure is a form of pressure that arises when circulating in the blood vessels. The heart and blood vessels play an important role in this process, where the heart is a muscular pump that supplies blood pressure to move blood, and blood vessels that have elastic walls and strong resistance (Hayens, 2003).

CONCLUSION

This study concluded that patients who took amlodipine had an average blood pressure of 145 mmHg and an average ureum level of 31.61 mg/dl. There was a significant effect between amlodipine consumption and ureum levels, with a p value of 0.003 (P<0.05). Future researchers are advised to explore the effect of creatinine levels in patients taking amlodipine. The results of this study can also be used as additional information and consideration for educational institutions in studying the effect of amlodipine consumption on ureum levels.

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